UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

ARBUTUS PHARMA CORP. et al.	**CIVIL ACTION NUMBER:**
Plaintiffs,	**23-cv-1876**
vs.	
PFIZER, INC., et al.	**MARKMAN HEARING**
Defendants.	**COURTROOM 4W**

Clarkson S. Fisher Federal Building & U.S. Courthouse
402 East State Street
Trenton, New Jersey 08608
Wednesday, December 18, 2024
Commencing at 10:34 a.m.

B E F O R E: **THE HONORABLE ZAHID N. QURAISHI,**
UNITED STATES DISTRICT JUDGE

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(PROCEEDINGS held in open court before The Honorable Zahid N. Quraishi, United States District Judge, at 10:34 a.m. as follows:)

THE COURTROOM DEPUTY: All rise.

THE COURT: All right, folks, have a seat.

Is there enough chairs?

All right, we are on the record in -- I don't know, is it Arbutus? I'm hoping I'm pronouncing that right, folks, but it's Arbutus Biopharma v. Pfizer, the docket number is 23-1876, for a Markman hearing.

Before we proceed, let me get appearances from counsel, and then we'll see if we finish the three and a half hours after that and we'll go from there.

MR. CALMANN: Good morning, Your Honor. Arnie Calmann for the plaintiffs.

THE COURT: How do you do?

MR. CALMANN: Before the introductions, I have to note, Your Honor, the new wave jury seats that you seem to have.

THE COURT: You like that? It prevents trials. I discourage trials in this courtroom by removing all the seats.

By the way, who put Mr. Calmann in the corner like that? That's good. I didn't see him.

MR. CALMANN: My co-counsel, who are really doing the work here, will introduce themselves.

MR. NIMROD: Good morning, Your Honor. Ray Nimrod from Quinn Emanuel, on behalf of plaintiff, Genevant. And with me today from Quinn Emanuel is Joe Paunovich.

MR. PAUNOVICH: Good morning, Your Honor.

THE COURT: Good morning.

MR. NIMROD: John Yang, and Joshua Burd.

And from Genevant today, Your Honor, Pete Zorn, who is the President and the chief legal officer, and Lindsay Androski, who is special counsel at Genevant.

THE COURT: Good morning to all of you.

MR. BRAUSA: Good morning, Your Honor, Adam Brausa from the Morris & Foerster Firm on behalf of Arbutus. I'm joined by the CEO, Mike McElhaugh, the general counsel, Chris Naftzger, the VP of investor relations, Lisa Caperelli, and the CFO, David Hastings.

THE COURT: All right. Good morning to all of you as well.

We switching sides here? What do we got?

MR. DENI: Your Honor, good morning. It's Bill Deni from the Gibbons Firm. I represent BioNTech.

MR. KLEIN: Good morning, Your Honor. Charles Klein, Winston & Strawn. We represent BioNTech. With me from Winston & Strawn is Alison King, Claire Fundakowski, Ivan Poullaos and Jovial Wong.

And with me from the client we have Raymond Parker

and Vinny Lee.

MS. FORMICHELLA: Good morning, Your Honor. Jessica Formichella from Walsh Pizzi O'Reilly Falanga, on behalf of Pfizer. And also with me from the Walsh Firm is Lauren Malakoff.

MS. TONNIES HORTON: And also for Pfizer, Sara Tonnies Horton and Heather Schneider.

And from Pfizer, Karen Chen.

THE COURT: All right, good morning to everybody.

Is that everyone?

All right. Well, then, look -- well, a couple of things. First of all, full disclosure, I presume I should at least inform the parties, I received the Pfizer COVID-19 vaccine. Anybody moving to recuse me? I will deny it, but now is your time. So if you want to move, feel free, but this is your opportunity. Otherwise, we're going to proceed.

All right, I don't see anybody standing up, so.

Look, I know you guys gave me a schedule. If anyone needs a break, I know this is a little bit of a marathon, I work through lunch. I probably got more communications about lunch in this case than I've ever received. If you all need a break, I will give you a lunch break. Otherwise, I'm willing to just go through and get the information that you guys are here to educate me on so that I can make an intelligent decision and give you an opinion in good time. But if you need

a break, I'll try to take some kind of break in the morning and break it up a little bit in the afternoon. But if somebody just needs a break for any reason, or counsel speaking for somebody else, just stand up and say, Your Honor, this might be a good time to take a 10 or 15-minute break. I'm going to give you that break at that time so you can stretch your legs or do what you need to do or just reboot. Okay?

What else? You guys already kind of put a plan together, right, on how you were going to proceed? You guys want to begin, give me my tutorial? How do you want to start?

MR. NIMROD: That sounds good, Your Honor.

THE COURT: All right, let's do that.

MR. NIMROD: Your Honor, I have three copies of our tutorial to pass up to you. You want paper copies?

THE COURT: Yeah, I need them. And also make sure -- Phil Gonzalez, my career clerk, is on my right. You got really two members of your audience today, so make sure that anything you're giving to me, Phil gets a copy.

MR. NIMROD: Here's a third copy, Your Honor.

THE COURT: You want to hold onto that, Phil?

MR. NIMROD: Good morning again, Your Honor. Ray Nimrod on behalf of plaintiffs in this case, Arbutus and Genevant, two companies that are pioneers in lipid nanoparticle technology, which is what we're going to talk about today.

The technology at the heart of this case is found in

the COVID-19 vaccine. The vaccine is made up of something called lipid nanoparticles, or LNPs. We'll get more into the background, but as a preview, it's important to note that there are two primary parts to the vaccine, a delivery vehicle and cargo. The delivery vehicle is the lipid structure. The type of lipid structure at issue here is made from a mixture of four types of lipids, which we'll get into. They assemble into a sphere-like structure during the manufacturing process, and the cargo is on the inside. Here, the cargo is mRNA, represented by the yellow squiggle. Lipids completely surround the cargo on the inside and also are on the outer shell.

I'm going to first discuss the cargo, Your Honor, the mRNA, and how mRNA vaccines are intended to be a function in the body.

So what we see here first is the COVID virus. Now, you don't want to inject with the vaccine the full virus, so scientists identify a part of the virus that is sufficient to train the immune system. For COVID, that was the spike protein, which you may have heard of, Your Honor.

Next, scientists determine the mRNA genetic coding for that protein. And before we go much further, Your Honor, mRNA simply stands for messenger ribonucleic acid. And the good news is, all we need to know for today is that the mRNA is the material that provides instructions to our cells about what proteins to make.

The next step is that the mRNA must be delivered into the cells inside the body. And this is the big scientific hurdle that hindered the development of RNA-based vaccines. We will be discussing this step later in the presentation.

The next step is that the cells then make spike proteins based on the coding from the mRNA and present them to the immune cells. The immune cells then become trained to look for and attack spike proteins. Then, when the actual virus enters the body, the trained cells can recognize and attack the actual virus that have the spike proteins on them.

And while this is a straightforward concept, the delivery part is a substantial challenge. And you don't have to take our word for that, Your Honor, Pfizer CEO, Dr. Bourla, stated and acknowledged the importance of delivery to mRNA therapeutics. He said, quote: The whole mRNA platform is not how to build an mRNA molecule, that's the easy thing. He goes on and says: It is how to make sure the mRNA molecule will go into your cells and give the instructions. That's the delivery part, get it to the cells, have it go in, and give the instructions.

So what are the hurdles with delivering mRNA? Well, first, mRNA by itself is fragile and can be destroyed in the bloodstream by enzymes and other immune cells. Second, mRNA cannot by itself enter into cells. It's not designed to do that. And third, packaged mRNA, if you put it in a package of

some sort, is useless if it gets in the cell and the mRNA does not get released, it needs to be released to do its job. Those were substantial hurdles and they held back mRNA therapeutics. In fact, in a 2003 article entitled, RNA To The Rescue, published in a prominent journal Nature, the Nobel Prize winning scientist, Dr. Phil Sharp, stated that the major hurdle for these kind of therapeutics was delivery, delivery, delivery. Now, after years of hard work, plaintiffs' scientists developed LNP technology that solved that delivery problem that Dr. Sharp identified.

Now let's just look quickly at the structure again. You notice how the mRNA is surrounded by lipids to protect it on the inside. Plaintiffs developed particular LNPs that overcame each of the three delivery challenges that we talked about. And let's talk about each one.

First, by encapsulating the mRNA in the lipid structure, the mRNA is protected from the enzymes and immune cells before entering the cells. Second, the lipid structure itself enables the LNP to enter into the cell, unlike naked mRNA. And third, once inside the cell, the LNPs released the mRNA. The reason is that the LNP is designed such that it holds the structure together based on the bloodstream's pH, but once it goes inside the cell, based on that difference, it releases the mRNA so the mRNA can do its job.

Okay. Now, Your Honor, let's discuss lipid

nanoparticles by breaking them down into their most basic parts.

Lipid nanoparticles, as the name suggests, are made from lipids. We interact with lipids all the time. They include things like fats, waxes. They're materials that don't dissolve in water. They are water repellent. There are many types of lipids, but some of the lipids that are very important to this case have special properties. One property is that they can have both a water-fearing or repelling end, that's shown on the left here, the tails. That's called hydrophobic. And they have a tail on -- a head, excuse me, on the right, that is water-loving, hydrophilic. And the result of that is that if you put these lipids into water, the tails don't -- will want to be near the water and the heads do not. Excuse me, the other way around. The tails want to be away from the water, so what happens is that they can form structures. Here we see the tails have faced towards each other and away from the water, and the heads are on the outside facing the water, which is where they want to be.

The patent specification here explains that there are a wide variety of types and sizes of lipid particles. The one we see here is called a micelle. Another type of lipid structure that you have seen in the briefs is called a liposome. Here there's water on the inside and on the outside of the particle, and there is a bilayer shown on the right,

Your Honor. The bilayer is made up of two layers where you have the tails facing each other on the inside and the heads on the outside. So the heads are facing the water, both on the inside and on the outside of the liposome.

Now, the arrangement of lipids in a liposome can attract nucleic acids. And we see that here in the figure where the squiggly line again is nucleic acid, and is sort of sticking to the outside of the liposome. And if you have a vial full of these things, then you can have a situation where nucleic acids get partially surrounded between liposomes, and those structures are called lipoplexes. However, lipoplexes do not work well as a drug. The nucleic acids are not protected.

So what was needed was to get the mRNA on the inside. And we see here again, we have the mRNA on the inside and a mixture of different lipids. But the question before all this LNP was developed was how do you get the mRNA on the inside, and what kind of lipid nanoparticle do you need to overcome all of the challenges of delivery into the cell? To answer these questions, plaintiffs' researchers had to identify the right type of lipids to use, the right amounts of each type of lipid, and a process and apparatus to manufacture the LNPs.

As we note, 2003 is when Dr. Sharp identified that delivery was the real problem here with RNA-based therapeutics. Arbutus's researchers worked for many years to solve that problem. They developed groundbreaking lipid-based

technologies to deliver nucleic acid medicines. Those efforts led to the first FDA-approved RNA-LNP therapy they called ONPATTRO in 2018. So it took a lot of time to get there, Your Honor. ONPATTRO uses a type of RNA called siRNA. And ONPATTRO was developed by Alnylam Pharmaceuticals using plaintiffs' LNP technology, delivery technology. They took a license and they're using plaintiffs' LNP delivery technology.

In 2018, Arbutus created Genevant and gave it a license to keep working on LNPs so that Arbutus could then focus on developing hepatitis B therapeutics. Today, Genevant continues to improve the LNP delivery platform. Genevant provides delivery technology working with collaborators. The collaborators provide basically the cargo, and they put their cargo in Genevant's delivery technology, the LNPs. Genevant has many collaborators, including BioNTech, one of the defendants here. The patents at issue here relate to Arbutus's groundbreaking work on LNPs.

Now, Your Honor, there are two patent families at issue, as you saw in briefing. One is one we call the lipid composition patents. I'll talk about that one first. That family has two asserted patents, a '359 patent and the '378 patent. They are directed to nucleic acid lipid particles composed of particular types of lipids at certain ratios. As such, the patents in this family are referred to as lipid composition patents. There are five named inventors, including

highlighted at the bottom, Ian MacLachlan, who we'll talk about a little later, he was the co-founder, chief scientific officer, and a team leader in the early days of the research.

Now, in contrast to the structures we saw earlier, the micelles and the liposomes, the inventors discovered that using four lipids in certain ratios was highly effective. Now, let's talk about each type of lipid that they discovered would be very useful to use in certain ratios.

First, we have what's called a cationic lipid. A cationic lipid is capable of carrying a positive charge. The positive charge has enabled them to attract negatively charged nucleic acids. Nucleic acids have a negative charge so the positive charge can attach to the negative charge.

Next, we have a conjugated lipid. That's a type of lipid that is a compound attached or conjugated to it such as we show here, it's polyethylene glycol, or PEG. The conjugated lipid helps prevent the LNP from sticking to other LNPs during the manufacturing process, and also helps the body -- the cell -- the LNP evade the immune system as it's making its way to the cell.

Next we have two structural lipids, phospholipid and cholesterol. And as their name implies, they play a key role in maintaining the structure of the LNP. And they are sometimes called non-cationic lipids to distinguish them from the cationic lipid on the left in the patent itself and in some

of the claims. So we have two structural lipids, two non-cationic lipids, phospholipid and cholesterol.

Okay. An important factor in the performance of the LNP and its lipid composition and the ratios lipids, not just the four here, it's the actual ratios and concentrations that are important as well, Your Honor. I'm going to take a moment to talk about the nomenclature and conventions for describing these ratios.

First, it's standard convention in the field to describe the amount of a lipid in terms of what are called moles. Moles are a unit of measurement that refer to a specific number of molecules present. The molar ratio in turn describes the ratio of 1 lipid to the total lipids present. An example here, Your Honor, a simple example here would be, if you have a particle which has two types of lipids in it, and the particle contains 1 mole of conjugated lipids and 3 moles of cationic lipid, you have 4 total moles present which means we could say that there's 25 percent of lipid A, that's 1 divided by 4, and then you have 75 percent of the second lipid, and that's just 3 divided by 4.

The scientists normally say mole percent rather than just percent by itself to clarify that we're talking about moles and not weight, Your Honor.

And the same concept applies when you have 4 lipids. In example 1 is just an example, in example 1 of the '359

patent specification states that there is 1.4 mole percent of conjugated lipid, 57.1 mole percent of cationic lipid, 7.1 mole percent of phospholipid, and 34.3 mole percent of cholesterol. And note that for any given embodiment, the lipid mole percents have to add up to a whole number, 100 percent.

Now, the lipid composition patents at issue in this case, there's two of them, and they are different. The first is the '359 patent. The '359 patent recites limitations A through D. Limitation A just requires a nucleic acid. The second limitation, B, requires a cationic lipid present comprising from 50 to 65 mole percent, that's stated to the nearest whole number, of the total lipid present in the particles. This one, importantly, as Your Honor notes from the briefing, has a lower limit of 50 percent stated to the whole number.

Then it goes on and says that there's a cationic lipid mixture comprising phospholipid and cholesterol, and the phospholipid has to have comprised between 3 to 15 mole percent of the total lipid, the cholesterol, 30 to 40 mole percent of the total lipid present.

And, finally, you have the conjugated lipid that it says inhibits aggregation of particles, we were talking about earlier. And its ratio is between .5 and 2 percent of the total lipid present in the particle.

So that's the '359 patent. As I said, there's a

second patent, Your Honor notes, in the family. And that is the '378 patent, claim 1. Claim 1 of the '378 patent also recites a nucleic acid particle. But there are important differences between the two claims. As you see, Your Honor, the '378 patent does not have a numerical recited limit for the cationic lipid. It simply states that it's a cationic lipid with no numerical limitation.

It goes on and says that there's a mixture of phospholipid and cholesterol, the structural lipids, from 30 to 55 mole percent. And what does that mean? Well, of course, if the embodiments covered here include up to 55 mole percent of the structural lipids, then such an embodiment at 55 percent could not have 50 percent cationic lipid because that would add up to 105 percent, which cannot be, of course. So the cationic lipid in that situation would necessarily be less than 50 percent. So that's an important distinction between the '378 claimed invention and the '359 claimed invention. The second important difference, Your Honor, is that the '378 patent uses the transition term "consisting essentially of", which Your Honor has read about, of course. And that is a disputed claim term we'll be discussing later.

I'd like now to turn to the second patent family at issue here. It relates to formulations, apparatuses, processes for achieving high levels of what's called encapsulation. That's just, you know, getting the mRNA inside the LNP instead

of the outside. And there are three patents in this patent family asserted in this case. They are the '651 patent. That's directed to formulations with high levels of encapsulation. We have the '320 patent. That covers an apparatus for creating LNPs with high levels of encapsulation. And the '098 covers a process for doing that.

The lead inventor on these patents was Ian MacLachlan, who we mentioned earlier. And, in fact, he's an inventor on both patent families.

So let's just look very briefly at claim 1 of the '651 patent. It recites a lipid vesicle formulation. As Your Honor knows, lipid vesicle is one of the disputed terms we'll be talking about in a moment. It also states in element (b) a messenger RNA wherein at least 70 percent of the mRNA in the formulation is fully encapsulated in the lipid vesicles. Other claims recite higher limits of 80 and 90 percent of encapsulation.

So these claims talk about percent encapsulation inside the particles. How do you measure that? Well, there's a well-known test that measures encapsulation efficiency. And I'll describe how it works at a high level.

So, Your Honor, imagine we just made a product with these LNPs in the lab. The ones that have circles with the squiggly line on the inside are LNPs with the mRNA on the inside. But you will see that there are other ones that do

not -- mRNA that is not surrounded by lipids, and those are on the outside, they're naked pieces of mRNAs that are free floating. So the question is, well, how do you determine how much of the mRNA of the total mRNA present is inside the particles versus the whole population as a whole?

Well, what you do, Your Honor, there's a test where you simply add a dye to the mixture. One example is something called OliGreen. And what it does, the dye goes and wherever it sees the nucleic acid, it lights it up. And so we see here, if you put a dye in, the dye can get to the free floating mRNA, but the dye can't get to the ones inside the LNP because they're protected. The dye can't make its way in. The lipids are stopping it just like they would help in the body, they were stopping the dye from getting to those mRNA particles. So all that lights up are the particles that are outside. So then what do you do? You take a measurement. You get a number down. That's called measurement A in this slide.

The next thing you do, Your Honor, is you add an ingredient that breaks open all the LNPs so the LNPs move away from the mRNA. So you put something in that does that. And now all the mRNA can be exposed to the dye. Put the dye in, take a measurement B. Measurement B is now calculating -- it's a numerical calculation -- the amount of mRNA total in the product.

So now you've got one measurement where you know how

much was outside, one measurement which is the total. And what you do then is you make a comparison. If you knew how much the total was, how much was on the outside, you can just do a simple subtraction and know how much was inside the particles, divide by the whole, and you can get them, the percent of mRNA that was fully encapsulated.

I want to note, this efficiency, this encapsulation, calculates the amount of mRNA that is encapsulated within the population as a whole. It doesn't look at strand by strand and tell you about the individual strands.

So as I mentioned, the second Arbutus patent family relates to obtaining this high encapsulation. These three patents that are asserted here, '351, is '320, and the '098. Along with the lipid composition family that we talked about earlier that talks about the four particular lipids and the molar ratios, they form the basis for the LNP technology that is used today throughout the history. Ian MacLachlan and the team at Arbutus solved the problem of delivery, delivery, delivery, that had been described by Dr. Sharp, that really plagued the idea of moving forward with these kind of therapeutics. And their delivery vehicle was ready when the world faced the COVID crisis in 2020.

In fact, Dr. Katalin Karikó is a scientist you may have heard of. She won the Nobel Prize for her work on mRNA in connection with the COVID-19 vaccine. She spent nearly 50

years of her career working with mRNA and it culminated in that vaccine. She worked with BioNTech developing their vaccine at issue in this case. And she was quoted in an article in Forbes magazine entitled, COVID's Forgotten Hero, as stating that: A lot of the credit goes to Ian MacLachlan for the LNP used in COVID-19 vaccines. In other words, she got the Nobel Prize for her work in mRNA, but she recognized that just as important to that was the work, not done by her, but done by Dr. MacLachlan and the folks at Arbutus to create the LNP delivery system.

And they titled the article, by the way, Your Honor, as, COVID's Forgotten Hero: The Untold Story of the Scientist Whose Breakthrough Made the Vaccines Possible. That's talking about Dr. MacLachlan. So Dr. Karikó was quoted as saying a lot of the credit goes to him. And then when the article came out, she Tweeted it and said: The LNP is as important as the mRNA in the vaccine. The part that she got a Nobel Prize for, mRNA. And she said LNP is just as important. And she credited Dr. MacLachlan and the team at Arbutus, which is in fact the case.

Your Honor, that concludes our tutorial, unless you have any questions?

THE COURT: I don't. And I presume the defense is going to provide some of sort of tutorial.

By the way, don't read my silence as anything more than -- when it comes to these tutorials, I actually care to

hear more from you than hear my own voice. So I'm paying attention to what you all have to say, but don't read my silence as indicating anything other than I really do want to hear from you folks, who are supposed to be the experts in this, trying to teach me how this methodology works. And so I appreciate it. I don't have any questions. But let me hear from the defense as well. It's my understanding that they're going to provide a tutorial as well.

Do you guys have slides for me also?

Kim, can you see what's going on?

(Sotto voce discussion.)

THE COURT: It's a new courtroom with new technology so this is expected. That's why we're still missing the juror seats, all of this has been redone, so.

Kim, if we need somebody, I can...

Why don't we do this, while she's getting someone, let's hold off on the tutorial for a few minutes. But I do have some questions. Let me just jump ahead for a minute and then we can come back too. But I'll get IT up here and we'll make sure that you guys can get your opportunity to speak with me.

But let me ask you just 30,000 feet above, and I don't know who's supposed to speak with the lawyers here, but where is the status of this case? How far have you been done in discovery? I want to get a sense of where this case is

since this case ultimately belongs to me, but I know you have been dealing more with the magistrate judge. So who can speak to that? How much discovery has been completed? What is left? And how long do we have? I'm just trying to get a sense of that.

MR. NIMROD: Your Honor, we have been doing -- we're at document production. We're at the tail end of substantial completion of document production.

THE COURT: And then you're going to go to the next phase. So how long is this discovery going to be? Look, I know there's no stay on this case, right?

MR. NIMROD: So the next step would be going through the documents and starting to take back depositions. We have a long ways to go, I would say, Your Honor.

THE COURT: Is there a schedule in place yet for the magistrate judge on how much time you guys have to get that done?

MR. NIMROD: No. But I believe, Your Honor, that it's left open until after your claim construction ruling.

THE COURT: And once I get that done, you'll get a schedule for your second phase of discovery?

MR. NIMROD: That's right, which should include a close of fact discovery, expert discovery, et cetera.

THE COURT: All right. But you're pretty much done with the documents; that piece of discovery you're at the tail

end?

MR. NIMROD: Yeah, there's some disputes, but yes.

THE COURT: All right. And with respect to this case, I'm going to presume that you haven't resolved any of these disputed claim terms between the filing of the papers and you guys coming here today, is that fair to say?

MR. NIMROD: That's correct.

THE COURT: And do I need to define a POSA for purposes of this hearing or no? Do I have to define a POSA?

MR. NIMROD: I don't think there's really a dispute there, no, Your Honor.

MR. KLEIN: No.

THE COURT: What other questions -- let me ask you this, do I need to go beyond the intrinsic record to construe these terms or can I be limited to that? What are the positions of both plaintiff and defense on that?

MR. NIMROD: Your Honor, there is some extrinsic evidence from our expert regarding, for example, the rounding issue. And the Court in the Delaware action which, looking at the same patents, relied I think pretty heavily on that. You know, the inquiry for claim construction, of course, is to look at things that they would be viewed by persons of --

THE COURT: Beyond that -- is that one expert?

MR. NIMROD: Yes.

THE COURT: Beyond that one expert, is there anything

else that you're asking me to take a look at?

MR. NIMROD: No, Your Honor.

THE COURT: And from the defense side?

MR. KLEIN: Your Honor, we don't think you need to go to extrinsic evidence.

THE COURT: Okay. All right, that's helpful. I didn't know you were disagreeing on that, but I want to make sure I understand and can kind of hammer down your positions on those issues while I'm trying to take a closer review of this.

What's the status, Kim, of our technology experts?

THE COURTROOM DEPUTY: Nobody is answering so I am emailing.

(Sotto voce discussion.)

THE COURT: All right. Folks, here's what we're going to do, because I need to get this tutorial. And I presume that even though I have the slides, it's better if it's presented on the screens.

We're going to take a ten-minute recess that allows the IT guys to come up. We'll try to work out this kink and you guys can stretch your legs, all right?

Remain seated, remain seated.

All right, thank you, folks.

(Brief recess taken at 11:08 a.m. until 11:27 a.m.)

THE COURTROOM DEPUTY: Please remain seated.

THE COURT: All right, we're good to go?

MR. POULLAOS: Good to go.

THE COURT: All right, you may proceed.

MR. POULLAOS: Thank you.

Thank you, Your Honor. Ivan Poullaos, on behalf of BioNTech and Pfizer for purposes of this hearing. And we're happy to present our tutorial.

So as Your Honor has already heard, there are two families of patents involved in this case. We are kind of calling them a little bit different things, so I put both names up here. On the left, we have the earlier family of patents, which we're calling the encapsulation patents, plaintiffs are calling lipomixer. Either is fine. But it's the earlier 2002 family of patents.

On the right, you have --

THE COURT: This is not a good sign. You guys couldn't even agree on a title that you were going to use for today's purposes? This doesn't bode well for where this litigation is going to be in a year or two, but okay.

MR. POULLAOS: We've put both up there just --

THE COURT: That's fair. We could follow.

MR. POULLAOS: And then on the right you have got the molar ratio or lipid composition. To be fair, I think those things are the same or similar things, but it's the later family of patents, and that's the 2008 family. Now, some of the terms appear in both, but some are unique to each family.

So let's talk a little bit about nucleic acid-based therapeutics. You have heard a little bit about this. I'm not sure that there's a lot whole lot of dispute here. But maybe just to put a finer point on things, nucleic acids in the human body, everyone has heard of DNA, the double helix, stores our genetic code, it's contained in our cells. And this slide here, we're just showing the process by which those instructions from DNA get carried out in the human body.

What happens is that the DNA opens up, it's sort of unzipped, and what gets formed is a single strand of RNA. And RNA is formed to carry the message, to carry the coded message inside DNA in the cell and to then execute its instructions and carry out the process that is coded inside the DNA.

And what happens then is that in the RNA, after what's called transcription where you get the RNA formed, the single strand, you then get a process called translation which is where the ultimate protein, or the substance that the body needs, starts to be formed. And you start with an amino acid chain, which then builds up and forms the protein. And what happens is that the amino acid chain gets built based on the instructions from the RNA. So the RNA, in essence, carries the message and the code to build up that amino acid chain. And once it gets built up, you have got a folding steps there where the amino acids fold in and create the protein. And it's the protein that then carries out the function in the body and is

released into the body to do its work.

Now, there are many different kinds of DNA and RNA. Our next slide, we have listed a few here. I don't think it's all that important right now to get into all the nitty-gritty details of them. But suffice it to say, you have got things like chromosomal DNA, that's the DNA we were talking about in ours cells, stores the genetic information. You have also got a type of DNA called plasmid DNA, and you will see the patents talk a bit about plasmid DNA. It's often found in bacteria. It's actually a circular structure, but it's a different kind of DNA.

And then on the right you have got various types of RNA. And we've listed a few there. You see we've got mRNA up there, which is obviously important for purposes of this case. But you do have other types of RNA as well that are listed.

Now, plaintiffs talked a little bit about this too, but nucleic acid therapy and nucleic acid-based drugs involves delivering to the body, delivering into the cells, a piece of nucleic acid, a piece of DNA, a piece of nucleic acid to then carry out its function in the cell. And what happens is that you can actually put a nucleic acid inside a lipid composition. And what that does is that it allows the nucleic acid to be delivered into the cell without being destroyed by the body. The body will recognize things as foreign substances and unless they are where they are supposed to be, the body will attack

them.

So you put it into the lipid composition and one thing that can happen is that you can then deliver the nucleic acid into the cell, the lipid particle gets taken into the cell where it then releases the nucleic acid, and then it can do its work that we just talked about, it can then form the proteins that the body needs.

Now, this type of therapy is used in various, various kinds of things. You may have heard of gene therapy, for example, where we supply -- doctors will want to supply a specific piece of DNA to a patient that has a genetic disease, is missing a piece of DNA or the DNA is not working right. This is one of the uses for nucleic acid-based therapy.

The other one that we're here to talk about today is for vaccinations. And, as you've heard, FDA approved Pfizer-BioNTech's COVID-19 vaccine and it was the first mRNA product ever approved by the FDA. And that was at the height of the COVID pandemic, as Your Honor knows. And how that works is that the vaccine carries mRNA into the cell. The cell -- that mRNA then carries instructions for the body to then make the spike protein in the COVID vaccine. So the COVID spike protein is made so that the body learns to recognize it and fight the real virus if and when it enters the body. So it's to mimic the actual COVID virus and build immunity to the real virus.

All right. So we'll talk a little bit now about the delivery of nucleic acid and the lipid composition. Now, you heard a little bit about this so some of this may be a bit repetitive. And I think we agree on certain things, but maybe not others.

So you've heard about lipids. And lipids are fats. And plaintiffs were correct, they talked about the lipid molecules at issue in this case, you will see a picture on the right, as having a non-polar end and a polar end. And that's what the patent talks about and what the literature talks about, is that they are amphipathic. Amphipathic simply means they have the fat-loving end and the water-loving end. Another way of saying that is to say that they have a non-polar end, which is the fat-loving end, and a polar end, one that is attracted to water.

And that's particularly helpful because oil and water don't mix. And so here you have a molecule that has both types of groups on it, a group that does like oil, a group that does like water. And so you have got an amphipathic molecule, is how that's described.

You also heard plaintiffs talk about the different kinds of lipid components and so I have listed them here as well. Now, these are lipid molecules, lipid components that were known in the art and were known to be used to make lipid compositions that could encapsulate nucleic acid payload. And

the various types that are relevant here are the cationic, or ionizable lipid, and that lipid helps to actually encapsulate the nucleic acid. You've got some helper lipids, a phospholipid as well as a sterol lipid, or cholesterol. And they form the structure. They help give the lipid particle some structure, the lipid composition position. And then you have got a PEG lipid. And the PEG lipid prevents the lipid composition particles from aggregating. It just keeps them from aggregating. It keeps them nice and homogeneous in the mixture because we don't want aggregation when forming these compositions. And then you have the payload, which is the active agent.

THE COURT: I'm sorry.

MR. POULLAOS: Yes?

THE COURT: Counsel, only because this does sound consistent with what I just heard from plaintiffs' side, will you be clear when there is a diversion to say, well, Judge, I know this sounds like what you just heard, and we agree with all these things, our pictures even look the same, right? But we're going to get to a point where you divert, you're going to make sure I'm clear about that, right?

MR. POULLAOS: I will be absolutely clear, yes, Your Honor. And I think it's actually important that we agree on some of this stuff because it will draw a sharper contrast as to where we --

THE COURT: No, I appreciate that. I just want to make sure. Because right now I'm not seeing the diversion. I know it's coming.

MR. POULLAOS: Yeah, that's right. The point here up till this point is that these types of things were known in the art. They were known as of 2002, which is the critical date that we're talking about for that earlier set of patents. And so this set of lipid compositions, the fact that you had lipids out there that could deliver nucleic acid, that was known, that was known, and the patent talks about that.

Now, this encapsulation, you also heard plaintiffs talk a little bit about what that means. And we agree, encapsulation means that you're protecting that payload from degradation. That's fine, so that it can actually get to the cell and do its work.

Now, you heard counsel, here's one where there may be a little bit of a -- maybe not disagreement, but just sort of flesh it out a little bit more, is that counsel for plaintiffs talked about one method for measuring that encapsulation. And you have heard him talk about the fluorescence test, which is number 2 on this bullet here. And this is our Slide 12.

Now, I think counsel explained it just fine, that is generally how a fluorescence test works. The point that we'd like to make is that there are many different detergents, many fluorescent dyes, many different ways of doing that test that

can alter the results. And there are other tests as well, fluorescence is not the only way to try and get a handle on this question of encapsulation, to try and measure it. All these tests measure something a little bit different. They're all trying to get to the same kind of thing, kind of answer, but they do measure it differently and they do give different results. And so you have got nuclease-based assays, and the patent does talk about that. You have got a fluorescence test, several different parameters you can adjust there. You have got gel electrophoresis, chromatography, radiolabeled assays. And all of those things can also be used to measure encapsulation. And I think plaintiffs' expert actually talked a little bit about those as well and said those are tests that can be used.

All right. So now let's talk about the types of lipid compositions existing as of 2002, because that's where we really start to get to the rub.

All right. Now, we actually used -- we borrowed some terminology from plaintiffs' expert here. He talked about the different types of lipid compositions that were in the patent. And he called the first sort of category the first generation. The first generation, the old type of lipid compositions that were used to deliver payloads. And those are aggregates, lipid aggregates. You've got an example such as a micelle. That's one example here. Another is a lipoplex. And he actually --

their expert had a very apt description of it. And it's actually supported by the literature. The literature actually uses this spaghetti and meatballs kind of analogy. And you can see it down here in the lipoplex. You have got what looks like a strand of spaghetti and some meatballs. And that's, you know, sort of a cartoon-ish way of thinking about how this first generation of lipid aggregates works. So that's the first generation.

And what the patent does is actually calls these up. And it says -- it gives the examples of micelles, which is shown right here. And it also gives the example of lipid aggregates. Lipid aggregates or micelles, the important thing there is that the encapsulated component, they're talking about the payload there, the nucleic acid, is contained within a relatively disordered lipid mixture. So think spaghetti and meatballs as kind of disordered, that's where the nucleic acid payload is. And that's kind of the first generation of lipid compositions. And so that's the important point to think about when you talk about these lipid aggregates or micelles.

So that was the first generation. The patent also talks about what we refer to now as the second generation. And these are things called liposomes or liposomes. And here is a bit about liposomes that I don't think you really heard much from plaintiffs, but which we think is very important to understand the context of these patents that we're talking

about and that we're going to be construing.

Now, what the patent says about this second generation, the liposomes, is that they are and they have an aqueous volume encapsulated by an amphipathic lipid bilayer. Now, that's the reason why I talked about amphipathic before. It just means the lipid that has the two ends, the polar and non-polar. But the important thing is that those lipids form what's called a bilayer. And you can see it here in the diagram we have. You have got the polar ends on the outside with the sort of the non-polar tails on the inside. And then you have got another layer that's kind of reversed. So the lipid particles -- the lipid ends sort of go together because they like each other. And the polar end, or the water-loving end, is attracted and points towards the water that's in the middle, that's in the core of this liposome. And that's what a liposome is, an aqueous volume or an aqueous core, a water core, surrounded by a lipid bilayer. That's the key feature of liposomes that the patent talks about. And the patent talks about them the same way that the literature does.

Here's a Genevant article by Eleni Samaridou. This is a Genevant article in the scientific literature as of 2020. So we're almost modern day here. And what they say is that the liposomes have an aqueous core, you have an aqueous core observed in the case of liposomes. That's what liposomes are. They have that aqueous core, kind of like a water bubble, water

droplet surrounded by a lipid membrane or lipid bilayer.

Now, the patent gives some examples. The patent talks about liposomes with multiple bilayers. They're known as multilamellar lipid vesicles, MLVs. And you see an example on the right here in a paper by Ian MacLachlan, whom you have heard plaintiffs talk about. So this is one of his scientific articles. And he talks about liposomes made of one or more bilayers. And you see the example on the left in that drawing. It's got several membranes, and in between each membrane is some water. So this can be helpful, as the patent explains, because you could have one of the outer bilayers sort of degrade away and then release a payload in that first water compartment. Then the second one could degrade away and release what's in the second water compartment, and so on and so on. So it's useful in that regard, but it's a multilamellar or multi lipid bilayer vesicle, MLV.

Now, you also have single bilayers and they're called unilamellar lipid vesicles or UVs. And then you have got small or large, so SUV or LUV. And that's what's shown over here as well. But they're all highlighted by the fact that they have internal aqueous compartments, an internal aqueous core.

All right. So another type of liposome that the patent talks about sort of in its -- and it gives three examples here, another type is what they call an SPLP, stable plasmid lipid particle, SPLP. And that is a type of liposome.

You see the patent actually says that, liposome vesicles of the present process are stable plasmid lipid particles, SPLP, formulations.

And, again, as with all liposomes, the SPLP represents a vesicle of lipids that has a reduced aqueous interior. Now, for SPLPs, the aqueous interior is a little bit reduced, and that's what the patent says. But make no mistake, it still has that aqueous core, that aqueous interior. Now, the reason it might be reduced a little is because you can see in here, and it's present in the name, plasmid, it contains a plasmid, that type of bacterial DNA, as the payload. So that's in the middle. So that plasmid is taking up some space. And, in fact, the plasmid itself kind of interacts with that lipid bilayer a little bit as well. So it kind of shrinks it in and that core is a little bit reduced. So they describe it here as having a reduced aqueous interior. And that's how the patent describes them.

And so these were the lipid compositions known in 2002 and described in the past. That's what they are, liposomes, lipid aggregates. And one example of a liposome is an SPLP, that contains a plasmid.

But now let's talk about lipid nanoparticles used today, all right, because it's different.

We've got a timeline here. And the 2002 priority date is that priority date of that earlier family of patents

that we talked about. Prior to 2002, as the patent explains, you have got all of these types of lipid compositions, LUVs, SUVs, MLVs, micelles, lipoplexes, SPLPs, et cetera. Those were all known as of the 2002 priority date.

But now what we've got is kind of the third generation of lipid particles today. Present day we now have lipid nanoparticles, or LNPs. And you heard plaintiffs talk about LNPs a lot, but didn't necessarily connect them to the patents that we're here to talk about. And that's because LNPs came later. LNPs came later.

And here's an example of what an LNP is. The main difference is that there is no aqueous core in modern day LNPs. So you heard about the liposomes that have the aqueous core in the middle, even the SPLP that's has an aqueous core, but modern day lipid nanoparticles do not. And that's a key difference. And I don't think you're going to hear plaintiffs dispute the fact that there is no aqueous interior in their lipid nanoparticle.

They put up a diagram or a demonstrative of an LNP, and we like that. This is slide 8 from plaintiffs. And it shows a modern day lipid nanoparticle. You've got the nucleic acid payload in the middle, and then lipids all around that payload, lipids. You didn't once hear them say that there's any water in that core, or that it's called an aqueous core, anything like that. It's just not. It's very different. And

these modern day LNPs were only recognized after this 2002 priority date, after the inventions that were claimed in this lipomixer, or encapsulation patents, were submitted to the Patent Office.

And it's not just us, right? Plaintiffs agree with us as well. Plaintiffs' expert testified to this at his deposition. And what he was asked was: Would a POSA reading the patent in 2002 understand that lipid vesicles would include LNPs used to deliver compositions?

And what Dr. Thompson said was: Yeah, prior to the '651 patent invention, people were working with liposomes but had not yet envisioned an LNP type of structure.

And that's our point. That's exactly right. They had not yet envisioned an LNP type of structure as of 2002 because it didn't exist. It wasn't appreciated. This is a new sort of third generation type of lipid nanoparticle.

And Dr. Thompson is not alone. Going back to Genevant's own article as of 2020, it says much the same thing. And here's what it says. It said: The LNP used today for nucleic acid delivery are quite different from classical liposomes. And perhaps one of the most distinctive differences lies in the fact that LNP do not display a lipid bilayer surrounding an aqueous core.

So that's straight from Genevant's mouth, in the scientific literature, and it agrees with their expert's

testimony in this case.

And so that's the point we want to make, is that LNPs are quite different. They have a lipid internal structure, not an aqueous internal structure such as the aqueous internal structures that the patents talk about.

And the Genevant article actually goes on and it says: LNPs exhibit similar structures with an electron-dense core, an electron-dense course, contrary to the aqueous core observed in the case of liposomes. And electron density, lots of lipids in that core. And that is different from the aqueous core observed in the case of liposomes. And it has to do with the fact that you use this ionizable lipid and it complexes or sort of interacts with that nucleic acid payload. And that's one thing that helps the LNPs to form, the third generation of lipid compositions.

So now let's talk about the asserted patents. We'll talk about that first family, the 2002 family, the encapsulation or lipomixer patents. And here are the claim terms that Your Honor is going to be asked to construe. You have got lipid vesicles, and then you have got the fully encapsulated term as well. And I think the background about liposomes and disordered lipid mixtures, that will all be relevant when it comes time to construe those terms.

But one thing you will not see in this earlier family of patents, in these encapsulation patents, is any example

where they are encapsulating mRNA in any of their particles. There is no example showing mRNA being encapsulated in any of those lipid compositions.

Another sort of contextual fact to keep in mind, is as we sort of alluded to earlier, the June 2002 priority date, that's when these patents were applied for, the application went in. And so that's the lens from which we need to view the patents. They are viewed by a POSA, person of ordinary skill in the art, at the time of the claimed invention. That's 2002.

Now, to be sure, this patent family has been kept alive for over two decades. Meaning, 20 years this family has been kept alive. And plaintiffs apply for more claims based on that same patent application, right. So despite the fact that you've got one of the patents, or two of the patents being applied for and granted after Comirnaty was granted, emergency use approval, after the COVID vaccine from BioNTech and Pfizer came out, you then had more patents being applied for. But despite that fact, we still need to look at them from the perspective of the person that's skilled in the art as of 2002. So that's the main point to keep in mind as we talk through these patents.

It's important to keep that in mind just because of the temptation to kind of tell a sort of a revisionist history story or narrative of the development of this claimed invention and what actually went on. And it's very tempting to interpret

old patents as somehow being relevant to new technology. And all we're saying is, Your Honor, we've got to keep that separate and make our focus in the correct time frame.

All right. Now, the patents also -- we're also disputing the term encapsulation. And here's a blurb from the patent that talks about encapsulation. It can refer to full encapsulation, partial encapsulation, or both. Those things are apparently different. But encapsulation, as I think we all agree, is the -- a nucleic acid payload being inside the lipid composition. That's what encapsulation is. And I think -- and then there's a dispute over what full or partial or even both means, but that's where that comes from.

So let's look to the second set of patents. This is the molar ratio patents. And here is our timeline here. This is our slide 30. This is the second family of patents. And they came later. They were applied for in 2008. So still before, well before the COVID vaccine was publicized and marketed and approved, and before certain disclosures about the vaccine were made. So they were applied for in 2008.

And you'll see here that at least one of the patents -- there are only two in this family that are asserted here -- but one of them, the '378 patent, was applied for after the COVID vaccine was released -- was approved. And, in fact, it was actually applied for after the disclosure to the world of the molar ratios of those lipids used in the COVID vaccine.

They were applied for after that was disclosed to the public. So this is again where we get into the temptation of trying to read patents that are applied for later in time after certain knowledge has become public knowledge in trying to import those into an earlier patent application.

Now, here are the claim terms at issue in that second family of patents, the molar ratio. We've got some mole percentage terms here relating to the cationic lipid and also the cholesterol, and you've got various percentages at issue. And then you have got the "consisting essentially of" term, and that relates to the '378 patent. And then you've also got "fully encapsulated," which appears in these patents as well. So that's one term that sort of applies across the board. All right. And you have the same kinds of disclosures about encapsulation in this patent family that you did in the first. And so --

THE COURT: I'm sorry, Counsel, just to be clear, "fully encapsulated" I know is a term that's in dispute. But earlier I thought you said "partial encapsulation" is also a term that's in dispute?

MR. POULLAOS: Our point is that the disclosure distinguishes between the two.

THE COURT: Okay. That, I appreciate. But the term that you're actually asking me to construe is "fully encapsulated"?

MR. POULLAOS: Correct. Correct.

THE COURT: Okay.

MR. POULLAOS: Thank you, Your Honor.

All right. Okay. Now, one other issue that Your Honor is being asked to resolve has to do with that "consisting essentially of" term. And what the law tells us there is that that term is construed with a view as to what the basic and novel properties of the invention are. What's the utility? What's the surprising advantage of the claimed invention? And that's what we're asking Your Honor to explain -- or to rule on. But the good thing is that the patent actually tells us.

The patent tells us what the advantages are of this claimed invention of the basic and novel properties are. And here's what it says, it says: There was a surprising discovery that in these lipid particles that are claimed, they provide advantages. And the advantages are increased activity of the encapsulated nucleic acid. So you're getting increased activity of that payload. You have improved tolerability of the formulations. That's another advantage that they tout. The patentees also tout the advantage of a significant increase in the therapeutic index. And that tells you how much of a drug you can give someone before you start seeing side effects. And here it says it's an increase in that window, that therapeutic index. And then the last one is that they are stable in circulation.

So those are the advantages that the patent talks about. And it actually presents some data in that regard. So this is from figure 1 of the patent, and it's example 2. So figure 1 provides the results that came out of example 2 of the patent. The important thing when reading this graph here is just remember, on the left-hand Y-axis here, the one that's going up and down, a lower number is better, a lower number is more potency.

And so what you see here is that you've got different ratios of cationic lipid, and some of the other lipids, different ratios, the one at the bottom is the one with the best. This is a 57 mole percent cationic lipid. And that was the most potent. And that's what the patent actually says, that's how they interpret these results. And it says: The 1 to 57, that 57, or first in the mole percentage of the cationic lipid, the 1 to 57 SNALP formulation -- and I'll talk about that -- was among the most potent. And here, SNALP, it's another term we haven't yet talked about, but this is a term that only appears in the 2008 patents, the later family. And it just means stable nucleic acid lipid particle. So another lipid composition where they are adjusting the ratios of these lipids, and they found that the 57 percent one was the most potent.

And so that is what they pointed to to support some of the advantages that they put forward for this claimed

invention. And so that's what they were talking about. And they explained this to the patent examiner as well. They said applicants have found that SNALP formulations have an increased amount of cationic lipid, from 50 to 65 percent, provide unexpectedly superior advantages, much higher potency or activity of the nucleic acid on the tumor, is what they were measuring here.

All right. One other point in this regard, Your Honor, is that the patentees had claims directed to that sentence that we just read. And here they're pointing to the ranges of these lipids. And one thing that happened was that in an earlier patent in the same family -- so it's still within the same prosecution history but an earlier patent -- there was a rejection by the patent office. And in order to overcome that rejection, based on the prior art, it was obvious it was a rejection, the patentees removed the word "about". So instead of reading from about 50 mole to about 65, it now just says from 50 to 65 mole percent. And that was an edit that was done in the application process in the prosecution history of that later family of patents.

And that's tied up in the point that the applicants made to the examiner about the basic and novel properties. And also, we'll be talking about this in the context of these ranges and how to construe those ranges.

So that's the end of our tutorial, Your Honor. Thank

you very much. I'm happy to answer any questions. But I think that will set up my partner to talk about these terms.

THE COURT: All right, thank you. I appreciate it. No questions.

What's next? Lipid vesicle?

MR. BRAUSA: May I approach, Your Honor?

THE COURT: You may.

MR. BRAUSA: And these are for all our terms.

Good morning, Your Honor. Adam Brausa, on behalf of the plaintiffs.

The first term we're talking about is lipid vesicle, which appears in three of the patents at issue. The parties actually agree that the same construction should be applied in all three patents. The parties disagree, as Your Honor is aware, about the meaning of this term.

Our construction comes straight from the intrinsic evidence, as you will see. The statement "lipid vesicle" means a lipid composition that can be used to deliver a compound. That's our proposal. It comes from the definition set forth in the specification. It's unambiguous, not in dispute, and we think this is dispositive on the term.

Through the tech tutorial and in defendants' brief you heard a lot about the examples and characteristics and configurations that follow this definitional statement. But you didn't hear much emphasis on the actual lead-in cause. And

it's important because it uses definitional language like refers to, and then it doesn't say we're talking about first generation, or second generation, or third generation, whatever those terms mean, those aren't used in the patent. It says: Lipid vesicle refers to any lipid composition that can be used to deliver a compound.

So I could stop there, but I would be remiss if I didn't address some of the arguments that you will hear in a moment.

THE COURT: That's fair.

MR. BRAUSA: But our view is, you don't need to go any further than this. It couldn't be clearer.

Now, we don't dispute that after this definitional statement, a non-exhaustive list of examples, characteristics and configurations of some lipid vesicles are used. How do we know it's non-exhaustive? How do we know that the definition of lipid vesicle should not be limited to these characteristics and exemplary configurations, which is what defendants' construction seeks to do. We know that because, again, the specification tells us. Before setting forth those examples, it uses language that tells us, again, unambiguously, these aren't limited, they're certainly included. These are characteristics and configurations of the claimed lipid vesicles, but they're non-exhaustive, they're not limited.

And, again, we could stop there. And in view of what

we heard just a few moments ago, that defendants don't believe any extrinsic evidence is necessary, I think we could stop there. But I think what you'll hear in a moment is that defendants' construction not only relies on extrinsic evidence, it's based on extrinsic evidence. Instead of dealing with this definitional statement, they go to a non-technical dictionary, the New Oxford American Dictionary, to import the word sac into the definition of vesicle. Sac doesn't appear anywhere in the intrinsic record. It doesn't appear in the specification. It doesn't appear in the file history. It doesn't appear in any technical dictionary having to do with lipids. This is an ordinary usage dictionary that provides examples in anatomy, zoology, botany, geology, and medicine. And they rely on this exclusively to put in the word sac into the proposal.

So this is incorrect and shouldn't be adopted for a couple reasons. First, it's not supported by the intrinsic record. You don't go to an extrinsic evidence when there's nothing left unresolved by the intrinsic evidence.

Second, what we'll see and what I suspect you will hear is that defendants' counsel in their briefing has suggested that the examples given are consistent with a sac containing an aqueous interior, or a relatively disordered lipid mixture. So they say, well, the extrinsic dictionary definition is consistent with the example. But, again, those are just examples. And nothing in the intrinsic record says,

well, to be a lipid vesicle you got to have an aqueous core, as we heard during that then and now portion of the presentation. Which, in my view, is really directed to an issue further down the line in this case, maybe written description, maybe non-infringement, but it doesn't have anything to do with what lipid vesicle means in the context of these patents as we saw in that express definition.

And we see their arguments in the briefs echo what we heard in the tutorial. This assertion that our expert, Dr. Thompson, whose testimony is unrebutted, and who, by the way, didn't actually opine on the meaning of lipid vesicle in view of the intrinsic evidence, but they argue in their brief that he admitted that as of that time frame the POSA had not yet envisioned an LNP type of structure. And then they go on to say: In view of Dr. Thompson's testimony, a person of skill in 2002 would not understand the scope of the claim term lipid vesicle to include LNPs.

So I think their point is laid bare here. They want to say our product is not a lipid vesicle because it's an LNP that doesn't satisfy our construction of lipid vesicle. But that construction isn't correct. It limits the embodiment. It limits the definition of vesicle when the specification in fact indicates it's a broad construction. It's any lipid composition. There's no support for that naked attorney argument because they didn't provide an expert in response to

Dr. Thompson.

And I'll note that when they showed the testimony, they at least showed the complete testimony in the slide. In their briefs, they omitted a key portion of Dr. Thompson's answer. And here we see it in completion where he said: Prior to the '651 invention, and then provided the testimony they quote. They omitted that "prior to the '651 invention" portion of his testimony.

If we turn back to the intrinsic evidence, which is dispositive on this term, it indicates that the specification of the '651 patent is, of course --

THE COURT: Sorry, Counsel, just remind me, which term or terms are you asking me to go beyond the intrinsic record? I know not for this.

MR. BRAUSA: So on molar ratio and fully encapsulated, the expert, our expert, Dr. Thompson, provides additional testimony on how a person of ordinary skill would understand the intrinsic --

THE COURT: Okay.

MR. BRAUSA: So it's a bit of a hybrid. He's not really going beyond it, he's providing interpretive guidance from the perspective of a person with skill.

If we turn back to the specification here where you don't need any testimony from Dr. Thompson, and indeed, he didn't offer any opinion on this term, the specification again

makes it clear that the examples of configurations and characteristics in that column 5 excerpt we saw, the definitional statement of a lipid vesicle, isn't so limited. The patent covers a wide range of lipid vesicle types and sizes, including lipid nucleic acid particles.

And if you look at their opening brief, when they talk about the background on LNPs, it's at page 3 of defendants' opening brief, they actually cite an article from 2000, not 2020. The then and now argument that we heard as part of the tutorial is just attorney argument. There's no expert that could back that up. And they had every opportunity to do so in response to our expert's declaration. But, frankly, it's inappropriate at the claim construction stage because the question before us is what a person of ordinary skill would understand based on the intrinsic evidence at the time.

The claims make this equally clear. And in the intended claim 9 we, again, the lipid vesicle could be a lipid nucleic acid particle. That's not in the list that defendants have focused on in the definition of lipid vesicle, but the claims and the specification make it clear that a wide variety of lipid vesicles are contemplated of varying size and characteristics.

Moreover, when Dr. Thompson, if Your Honor is interested, what he actually testified to when asked point

blank: Hey, how would a person understand this portion of the specification? Would a person reading the '651 patent understand that an LNP such as the one on page 10 -- and this is the LNP that was referred to as generation three -- would they understand that to be a lipid vesicle in the context of the '651?

And he answered as unambiguously as the definition in the specification: Absolutely.

And so for that reason, Your Honor, we would submit that plaintiffs' construction of this term based on the intrinsic evidence should be adopted.

THE COURT: All right. Thank you, Counsel.

Again, we're going to alternate, right? We're not going to do all the terms in the complaint, we're going to go one by one?

MR. BRAUSA: That's my understanding.

THE COURT: It's helpful to me if we do it that way. So I'll hear from the defense on lipid vesicle.

This is for all the terms, right?

MR. KLEIN: I believe so.

THE COURT: Okay.

MR. KLEIN: Lawyers love their slides.

THE COURT: It's helpful. I will tell you, I'm actually a fan of the PowerPoint. I actually think it's helpful in educating me on your positions. Reading through the

briefs are helpful, but you have to do it numerous times. And this sometimes condenses the issues and disputes. So I just want to make sure this wasn't all for one term, then it may not be as helpful.

MR. KLEIN: Understood.

THE COURT: All right.

MR. KLEIN: Thank, Your Honor. Charles Klein, Winston & Strawn. I will be presenting for the defendant.

Let's go straight to slide 5. Looks like I have control here.

Plaintiffs' argument, Your Honor, did not address the core dispute. They didn't address the core dispute, which is pretty straightforward. Do you construe lipid vesicle from the perspective of a skilled artisan back in 2002? That's our position. Our position is you construe that term based on how a skilled artisan in 2002 would understand. Plaintiffs' construction includes not only what a skilled artisan knew in 2002, but what a skilled artisan knows today. Look at their construction. A lipid composition that can be used to deliver a compound. No time limitation. Doesn't say a lipid composition known to a skilled artisan in 2002 that can be used to deliver a compound. This will confuse the jury. The jury will think that any lipid vesicle used today is a lipid vesicle used two decades ago in 2002.

Our construction is consistent with the intrinsic

record. Like I said earlier, I don't think you need to go to extrinsic evidence. And our construction covers the lipid compositions that were known as of 2002.

And just briefly I'll address the term sac. Your Honor, the term sac is not important to our construction. You could swap that out for lipid composition. It's just a descriptor. The point is, the point of our argument is lipid vesicle has to be construed from the perspective of a skilled artisan as of 2002 in view of the intrinsic record.

And as we explained during the tutorial, this is important, the distinction between 2002, what was known in 2002 and what's known today is important to this case because the lipid nanoparticles that are used today were not known as of 2002.

Plaintiffs try to rely on the answer from their expert, Dr. Thompson, when he was asked about whether a POSA reading the patent in 2002 would understand lipid vesicles would include LNPs that are used to deliver compositions. They were clearly expecting a yes because they asked that question. It's the very last question in the deposition. They were expecting a yes. They didn't get a yes. And they got: Prior to the '651 invention there was the LNP. And then he starts, you know, stream of consciousness: People were working with liposomes, or had not yet envisioned an LNP type of structure.

That's true not only prior to the '651 invention.

The specification does not describe the type of lipid nanoparticles that are used today, it just doesn't. And I'll talk about that.

And, again, during the tutorial we mention this Samaridou article sponsored by Genevant itself from 2020. This is Exhibit 35. And this article distinguishes the LNPs used today from the classical liposomes saying they are quite different, and LNPs do not display a lipid bilayer surrounding an aqueous core. You will not see any discussion in the specification about LNPs used today or, you know, an advancement from the classical liposomes.

Now, fortunately, Your Honor, there is a seminal federal circuit en banc decision that resolves this dispute, and that's *Phillips*. And as I'm sure Your Honor knows, the point of construing a patent term is to ascertain the ordinary and customary meaning of the claim term. And that's the meaning the term would have to a person of ordinary skill in the art in question at the time of the invention in the context of the entire patent, including the specification. That's a legal standard we've all seen hundreds of times. And the only exceptions are disclaimer and lexicography. And those exceptions don't apply here.

To be sure, Your Honor, I'm on slide 9, there is a definition of lipid vesicle in the patent. And believe me, I'm going to talk about that definition. But what's important is

in their responsive brief at page 4, plaintiffs concede that their construction is based on that definition. But in their view, the definition is consistent with and not a departure from the plain and ordinary meaning of the term.

So the Court should apply *Phillips*. The *Phillips* standard applies. A lipid vesicle should be construed from the perspective of a skilled artisan as of 2002.

So this is what plaintiffs are doing. They take the first part of the definition and they say: Lipid vesicle refers to -- they say a, but the patent actually says any -- lipid composition that can be used to deliver a compound. And they say: That applies to any lipid composition known today. But this was written in 2002. This is referring to any lipid composition known to a skilled artisan in 2002. And then they say don't look at the rest, don't look at the rest of the definition. No question, Your Honor, the rest of the definition is describing examples. And it says: Including but not limited to. We're not fighting with that. But we did cite a case, the *Shire* case, that talks about multi sentence definitions and says: A term may be defined by what it is, what it may be, what it is typically, and the patentee-included important definitional information throughout the entire paragraph. And that's what we have here. If you look at the entire definition, lipid vesicle is referring to any lipid composition. And under *Phillips*, that means any lipid

composition known to a POSA as of 2002. It's not talking about future-invented, future-discovered lipid compositions. And we know that because when you look at the examples, the common factor in these examples is that the lipid compositions either have an aqueous interior, or a relatively disordered lipid mixture. We're not saying the examples limit, limit lipid vesicle, but they provide important definitional information as to what types of lipid compositions were known as of 2002.

And as *Phillips* says, you look at the entire patent. And the entire patent includes another discussion of lipid vesicles in column 6 and 7 -- we're on slide 13, so it's column 6, line 63, to column 7, line 4. And here, the specification is talking about lipid vesicles. And it describes some lipid vesicles that are not actually part of the definition such as SUVs, LUVs, MLVs. They're covered by the definition, but they're not specifically described in the definition.

And then, importantly, the inventors say: Those of skill in the art will know, they will know of other lipid vesicles, will know as of 2002. You won't see anything in the specification saying, oh, and by the way, our present invention works for lipid vesicles that no one's thought of yet, no one's invented yet, no one's discovered yet. You don't see anything like that. The lipid vesicles may be -- the definition may be broad, it may cover any lipid vesicle, but only the lipid vesicles that were known as of 2002. And that's the point.

That's the core point of our construction.

And so what was known as of 2002? When you go through the specification, Your Honor, you see -- and I'll go through this quickly because it was covered in the tutorial, but you have this first generation lipid aggregate. And these are relatively disordered mixtures. I don't believe any of this is disputed. You have got the micelles or lipoplexes. And then you've got the second generation, which is really the focus of the patent, or the liposomes or liposomes, and they all of aqueous interiors, LUV, SUV, MLV, SPLP, has got an aqueous interior.

Plaintiffs' expert -- again, we don't think you need to rely on its expert -- but plaintiffs' expert says a POSA would understand that there are two different potential locations of the encapsulated nucleic acid, either within a relatively disordered lipid mixture, or in the interior. And what does he cite? He cites the portion of the patent where there's a definition of lipid vesicle and he's citing the examples, the portion that plaintiffs say don't take a look at.

Plaintiffs rely on Dr. Thompson's testimony that a POSA would understand an LNP to be a lipid vesicle in the context of the patent. But that's as to the present tense. Would a POSA understand? That's not the right question under *Phillips*. The question is, would a POSA understand in 2002 that an LNP used today, which wasn't even known in 2002, was

part of the invention? The answer is no. Plaintiffs eventually asked that question and they didn't get a yes.

THE COURT: I get the argument.

MR. KLEIN: That's the end of the argument.

THE COURT: Yeah.

MR. KLEIN: The point is, their construction, Your Honor, has no time frame.

THE COURT: I got it. It's like predicting the future. By the way, my questions -- I'm sorry, if I misstate someone's name, it's because I'm not tracking as well. Is it Mr. Brausa?

MR. BRAUSA: That's correct.

THE COURT: Did you handle the lipid vesicle? We just addressed this. What is your response to Mr. Klein's argument that, look, it says any lipid composition, but doesn't it have to be known to a POSA back in 2002? It can't be some crystal ball that says, well, if something is not known in 2002, but if we figure it out in 2020, that's covered by this patent. And, by the way, would you concede that that shouldn't be how that's interpreted?

MR. BRAUSA: So I would concede, and I think we agree, rather, I don't think it's a concession, *Phillips* is the law, and it says you construe things at the time of the invention.

Where I think we fundamentally disagree is what the

appropriate inquiry is at claim construction. At claim construction, you look to the intrinsic record, you look to what it says the definition should be, and you don't look to the future without any expert testimony, without any support for the statement, and only extrinsic evidence in the future to contradict and narrow the definition of lipid vesicle to something that we fundamentally believe a POSA would recognize looking at the disclosure of the patent.

But, again, that's a decision separate from claim construction. We're looking at what the patent says, the intrinsic record. Those words are written in 2002. And so that's dispositive. If it were otherwise, and you were always looking into the future, you would be having many trials and expert depositions on the 20 years that fall.

It's very often in the case that terms of patents encompass things that are developed after the words on the page are written. And here, as we saw, the intrinsic record fully contemplates it. The POSA will know of other vesicles. Lipid nucleic acid particles are called out in the specification and the claims. In plaintiff's brief, again, opening brief, page 3, on the background of LNPs, they cite an article from 2000 and they say this is just a lipid nucleic acid particle, it encapsulates that.

So while we agree that the proper legal inquiry is to look at this from the perspective of the --

THE COURT: You're saying it includes what they're saying is precluded? You're saying this was known back in 2002?

MR. BRAUSA: That is correct. And, moreover, even if Your Honor has questions about that, that's a validity or non-infringement issue, it's not a claim construction issue.

THE COURT: All right. I appreciate it.

Are we on the next term, folks?

I'm sorry, Mr. Klein, you want to say something?

MR. KLEIN: Yeah, very quickly, Your Honor.

THE COURT: All right.

MR. KLEIN: I'm going to make a suggestion that if you were to adopt plaintiffs' construction, you would change it to a lipid composition known as of 2002 that could be used to deliver a compound. Otherwise, the jury is going to be confused. This is going to confuse the jury.

THE COURT: All right. I appreciate that.

You want to respond briefly? Because we got a couple other terms, folks.

MR. BRAUSA: Sure, sure.

THE COURT: All right. What's your response to that? That it's not necessary?

MR. BRAUSA: I would say I disagree that adding as of 2002 things that were known will help a jury understand what a lipid vesicle is. Moreover, there's a whole body of case law

in the 112 context of after developed technology. Again, this isn't a claim construction issue. These are validity, non-infringement arguments masquerading as a claim construction argument. And I think that's indicated by the emphasis they put on sac in their briefing, and now they're saying, oh, it doesn't have to be a sac. As long as they can try and preserve that invalidity or non-infringement defense, that's obviously the goal, I think. That's not claim construction.

THE COURT: All right. I appreciate both your responses.

Fully encapsulated. Who's up next?

MR. BRAUSA: It's me again, Your Honor.

THE COURT: All right. It's easier, I don't have to remember so many names. Just give me one speaker, guys. Oh, you're going to tag team?

MR. BRAUSA: I'll try and keep this one brief.

THE COURT: We'll probably address one more term and then we'll take a break. If you tell me we need a break before then, I will absolutely give it to you. But right now I want to see if we can get through fully encapsulated.

MR. BRAUSA: Understood.

Fully encapsulated, as we heard, it appears in two different patent families. Again, the parties fundamentally agree that the same construction, in our view, or not in defendants' view, should be applied.

In one of the patents there's a -- the claim term refers to the percentage of mRNA in the formulation of being fully encapsulated, so that's talking about the total population of mRNA in the full -- in the formulation.

The other patents talk about the either nucleic acid RNA or mRNA, depending on the claim, being fully encapsulated in a single nucleic acid lipid particle.

I'm going to start with the '651 because I think that illuminates really what it means to be fully encapsulated. And we see that term in the claim 1 of the '651 patent, and then we see the dependent claims which add on higher and higher levels of full encapsulation.

Our proposal is relatively straightforward. In our view, based on the intrinsic evidence as interpreted by and explained by Dr. Thompson, that's referring to the location of the nucleic acid. And when you have the percentages, it's the amount of nucleic acid or mRNA that is contained inside the lipid vesicle, as opposed to within this disordered lipid mixture that we'll talk about in a moment.

I think it's fair to say that defendants' proposed construction has evolved over time. Initially they proposed that in this patent the term was indefinite. They then proposed a few days before opposition briefs were due that the parties should agree to the ordinary meaning of the term. And then, after further consideration, we're back to indefinite.

We think there's a right decision for the Court. We're certainly aware of Your Honor's order saying that indefiniteness will be decided at a later stage in the case. And, again, this is a claim construction dispute. There is a ripe dispute about what the term means. And you will hear a lot about what partial encapsulation means. Your Honor's question about whether the term was fully encapsulated or partially encapsulated anticipated some of the argument, because the term is fully encapsulated.

And so that's the question before the Court to resolve. And based on the intrinsic record, we'll see that the inventors, Dr. MacLachlan and his colleagues, repeatedly through the patent and through the prosecution history distinguish their invention, and the mRNA contained inside the vesicle from prior systems where the nucleic acid was within a disordered lipid mixture, but not actually inside the vesicle.

And we see in the specification of the patent it talks about the therapeutic agent, the nucleic acid, being trapped within the lipid vesicle. We see similar disclosures talking about encapsulation in the formed vesicle. And then after these disclosures, or accompanying them, you see there's discussion of encapsulation efficiency. And that's where the percentages come from. And the percentages set forth in the specification track the claim. And that's important because, as we'll see in the file history, and this is made abundantly

clear, encapsulation efficiency is the term used as a proxy for how much full encapsulation you have got. What percentage of the mRNA, or nucleic acid in the formulation, is contained inside the vesicle? And that can be determined by the fluorescent dye assay that my colleague Mr. Nimrod talked about earlier.

We also go back to the definition of lipid vesicle, which was alluded to in the tutorial by defendants' counsel because it provides characteristics and configurations of lipid vesicles, including different locations for the nucleic acid. We see that it can be contained inside the lipid vesicle and particle, or it can be encapsulated within a disordered lipid mixture. And these types of configurations were known in the art. You see this here where the nucleic acid, the strands, are outside of the lipids, they're not inside the lipids, but nonetheless, they're sort of within that mixture.

Now, for me, these two dimensional representations don't really give me a full mental picture and so I did a little digging before the hearing and found a good example of a feature at the Philadelphia Mall in 2022. And you can think of this configuration similar to these ball pits, which I was surprised to learn after COVID are still around.

THE COURT: I'm surprised they're around pre-COVID, to be honest with you.

MR. BRAUSA: Nonetheless, you can see here the point

which is that, of course the kids are kind of immersed in these balls, they're contained within the mixture of them, but, of course, they're not inside them. And that's what you can picture the disordered lipid mixture as being similar to.

So we see here two different locations being referenced. And then in the immediately following paragraph we see a reference to full encapsulation and partial encapsulation. And, in context, as Dr. Thompson explained, the POSA, or person of skill, would understand this reference to full and partial encapsulation to be in reference to the different potential locations of the encapsulated nucleic acid. Partially encapsulated is within a disordered lipid mixture. Fully encapsulated is actually inside the vesicle or the particle.

Dr. Thompson's testimony on this and how a person of skill would understand the specification is unrebutted. They had his report. They took his deposition. They could have provided an expert saying, no, no, no, no, that's not how a person of skill would understand it, and they didn't.

And so based on the intrinsic record, we have this distinction drawn in the specification between fully encapsulated, contained inside on the left, and partially encapsulated, within a disordered --

THE COURT: Just to be clear, though, Counsel, you keep saying intrinsic record, but you want me to consider

Mr. Thompson's testimony, correct?

MR. BRAUSA: I do. But he's interpreting the words on the page. It's fair, yes. In order to --

THE COURT: I just want to be clear, you're not asking me to ignore it and just focus on the intrinsic record?

MR. BRAUSA: -- contrast the lipid vesicle, but you don't need to consider it --

THE COURT: The point is that, look, all the expert's doing is reading what's on the piece of paper and saying this is what a POSA would interpret it to be, and that's your --

MR. BRAUSA: You got it.

THE COURT: Understood.

MR. BRAUSA: And that brings us to the *Moderna* Court's construction of this term, which draws a different distinction between fully and partial encapsulation. And here we see that the *Moderna* Court construed effectively partial encapsulation to mean partially contained inside. And that's sort of a lay person's understanding. You can see how the Court might get to this opinion because if you think about something being fully encapsulated or partially encapsulated, you didn't know anything about the science or the specification, you can see where this would come from.

Couple things about this. One, it's based on a strand by strand approach. You're talking about individual mRNA strands, not the population of mRNA as a whole. Two, it's

inconsistent with the intrinsic record. This was attorney argument raised by *Moderna* at the hearing, and we disagreed that this is actually the distinction between full and partial drawn in the specification. The specification, nothing talks about the concept of a mRNA that's somehow half in/half out of a vesicle, and there's no disclosure saying that partial encapsulation means partially contained inside. Moreover, as Your Honor recognized, the term we're construing is not partial encapsulation, it's full encapsulation.

And, finally, one fundamental difference between *Moderna* Court's construction and this case is we have additional evidence. Again, this is extrinsic evidence from Dr. Thompson who was asked pointblank: So what about this situation of a nucleic acid that's partially in the particle and partially outside the particle?

And he says: These aren't thermodynamically stable. There's some kind of short time scale event during initial formation. Effectively, they don't exist.

So, respectfully, Your Honor should not follow, or we would ask that Your Honor not follow the *Moderna* Court's construction in view of this new evidence in the record and because it's inconsistent with the explanation of the intrinsic record provided by Dr. Thompson.

Now, again, defendants aren't challenging. They didn't come forward with an expert saying, no, Dr. Thompson's

wrong. And, importantly, they're not advocating for the *Moderna* Court's construction either.

The distinction between partial and full encapsulation drawn in the specification is also reflected in the file history. And that's yet another reason that we'd ask the Court not to just follow the *Moderna* Court's construction on this term. And when we turn to the file history, what we see is this claim as originally filed had included this fully encapsulated term. And in explaining what these claims meant, to distinguish over this prior art, which we talk about in our brief, the applicants clearly explained that here we've got encapsulated mRNA within the lipid vesicles, not mRNA merely associated with the surface of a preformed liposome. This is the lipoplex you heard about, the relatively disordered lipid mixture.

As the claims go on, or as the prosecution goes on, rather, we see that the percentages get introduced. And then when we're talking about the percentage of full encapsulation in the claim, the applicants and the examiner alike understood this to be a proxy in reference to encapsulation efficiency. The claim's talking about a percentage of full encapsulation. When describing these claims and distinguishing over the prior art, the applicants refer to the minimum encapsulation efficiency required by the claims in the present formulation.

Again, as we'll talk about in a moment, and as

Dr. Thompson testified, a person skilled would know that the way to do this is by applying one of these fluorescent assays; that is, measuring how much mRNA is contained inside the vesicle.

We see the same thing as prosecution goes on. And then we actually see a rejection where the examiner arrives at the same conclusion. And so both the applicants and examiner alike understood that fully encapsulated in the claims is determined by encapsulation efficiency. That's significant because I don't think there's any dispute encapsulation efficiency is measuring how much nucleic acid is inside the particles. And so that's additional confirmation of this distinction drawn in the specification.

Now, for the '359 and '378 patents, we have similar construction. Here it's on a particle basis. Again, I think it's fair to say that defendants' proposal has evolved. Initially they said that in these patents, but not in the '651, there was lexicography. That definition is here, we'll see it in a moment. Then they proposed, no, let's go with ordinary meaning instead. And then ultimately settled on indefinite.

The intrinsic evidence here is again consistent and supports the construction contained inside, talks about fully encapsulated being within the lipid portion. You can see that again here talking about full encapsulation within. And then the '359 patent and the '378 actually include an express

disclosure that you determine full encapsulation by an OliGreen assay, once we saw that inside a test that we talked about previously.

Turning to Pfizer and BioNTech's arguments. There are three. One is that there's lexicography. I think that's been withdrawn in view of the evolution of the construction. I will touch on it --

THE COURT: Well, has it been withdrawn?

MR. KLEIN: It's been withdrawn, Your Honor.

THE COURT: All right, so then we can skip.

MR. BRAUSA: Then we'll just blow right to number two.

THE COURT: See that? I'm all about efficiency, right?

MR. BRAUSA: I will try and encapsulate.

In number two, the POSA would not know how to measure fully encapsulated. You heard an illusion to this in the tutorial that there were multiple tests available.

And then three, the critique that our construction gives no meaning to the term "fully", that we're just reading fully out of the claim.

Skipping through number one, yes, we have testimony from Dr. Thompson saying a POSA would know how to measure full encapsulation. Here's the test. Use it -- or you utilize a dye that's fluorescent. And my colleague Mr. Nimrod explained

how that worked.

There are other portions of his deposition testimony where he's asked about the other methods that defense counsel alluded to. And he testified, in fact, that by 2002, it settled on a dye-based assay from the perspective of a person of ordinary skill.

Moreover, this question again of, well, which method do you use? That doesn't really tell you what the meaning of full encapsulation is. This is another example of previewing a potential invalidity argument. Maybe it's indefiniteness, maybe it's written description, maybe it's one -- or even non-infringement. I'm not sure. But that has nothing to do with what fully encapsulated means. The construction does not require a particular assay. It requires a specific location and structural configuration that is described in the specification.

So a person of ordinary skill, based on the testimony of Dr. Thompson, would in fact know what test to use. But, again, I don't think the Court needs to actually reach that issue because it doesn't have anything to do with the meaning of what it means for a nucleic acid to be fully encapsulated. And, again, the testimony is unrebutted. In his report, he again points to the specification that I talked about. I won't belabor the point, but he goes on to say that a POSA would know how to do this test and would know that it's measuring full

encapsulation.

The last point I want to make briefly is that our construction, hopefully Your Honor recognizes by now, does give meaning to the word "fully". It reflects the distinction drawn in the specification. You see on the left, fully encapsulated is contained inside, partially encapsulated is within a disordered lipid mixture.

Dr. Thompson's interpretation of that from the lens of the perspective of a POSA is unrebutted. And, again, we think it's dispositive on this term. And so for that reason, we would ask that Your Honor adopt plaintiffs' construction for fully encapsulated across all three of these patents.

THE COURT: All right. Thank you, Mr. Brausa.

Mr. Klein, you're back up?

MR. KLEIN: I'm back up. I have got all four terms, Your Honor. Keep it easy.

THE COURT: Before we do anything, I'll give you an opportunity, do you want to address why you don't have an expert? I mean, look, Mr. Brausa has mentioned more than one time, unrebutted, unrebutted. I'll at least give you an opportunity on the record to explain why it was unnecessary, if that's your position.

MR. KLEIN: Yes. Yes.

Can we put up slide 20?

There's a very simple explanation, Your Honor.

THE COURT: We got to switch over, right?

MR. KLEIN: If you look at our construction, our construction is indefiniteness. That's our construction. Your Honor entered an order, has it in a later slide, saying don't argue indefiniteness at this claim construction hearing. So we don't have an expert talking about whether different measurements would have different results or anything else related to indefiniteness, because it's premature.

THE COURT: All right. I appreciate that. But I wanted you to have an opportunity to at least respond to it.

MR. KLEIN: Thank you.

And so the core dispute here is not indefiniteness. That will be at a future point in time. The core dispute is whether contained inside is a proper construction for fully encapsulated given that the patent distinguishes fully from partially. That's the issue. That is the issue.

And if -- we rely on the intrinsic record. Plaintiffs' point to their expert, but their expert is what they rely on to explain fully versus partially encapsulated. The specification, the intrinsic record -- and it's virtually identical in both families -- on the left we have the '098 patent, column 5, lines 47 to 49, and on the right we have the '359 patent, column 11, lines 59 to 62. And they say: Lipid encapsulation can refer to a lipid formulation which provides a compound with full encapsulation, partial encapsulation, or

both.

And our position is the intrinsic evidence leaves at least three questions totally unanswered. How are full and partial encapsulation different? You saw the demonstrative with the kids in the balls. Are the kids partially inside the balls, encapsulated in the balls? Are the balls partially encapsulated in the kids? I didn't understand the demonstrative. I don't understand what partial encapsulation means. And there's no explanation in the patent. How do you measure full versus partial encapsulation? And how can a compound be both fully and partially encapsulated? I didn't hear any explanation of that. And so the intrinsic evidence leaves these types of questions unanswered.

And in the *Moderna* decision, the Court there talked about how there were multiple portions of the specification that support distinguishing between fully and partially encapsulation, and said: The inventors' decision to refer to full and partial as alternatives confirms that when they use the word "fully", they intended to exclude the word partially. And that's why in the Court's construction, the Court added fully as distinct from partially contained inside the lipid vesicle. If Your Honor wanted to adopt that construction, we don't have an objection because our defense is indefiniteness. Again, as I mentioned a moment ago, we're not addressing indefiniteness because you told us not to.

And so our argument is really very simple. Encapsulation means contained inside. The term here is fully encapsulation, fully encapsulated. And they're reading fully out. They're just saying fully is mere surplusage. And we cited the *Biocon* case's proposition that claims are interpreted with an eye toward giving effect to all terms in the claim. You're not supposed to treat a claim term as mere surplusage. And that's our point. They have construed encapsulated. They haven't construed fully encapsulated.

And with regard to this concept of encapsulation efficiency and measuring encapsulation efficiency, that could be the concept addressed in the claim, but the claim term is "fully encapsulated". And the Moderna decision addressed this same argument by plaintiffs and said, the disputed term is not encapsulation efficiency as used in the specification, but rather, fully encapsulated.

And so, Your Honor, that's our argument. It's very straightforward.

THE COURT: I appreciate that, Mr. Klein.

All right, folks, why don't we -- I'm going to keep to my promise -- oh.

MR. BRAUSA: I have two minutes, Your Honor, if you'll indulge me?

THE COURT: I'll indulge. But then we're going to take that break.

MR. BRAUSA: Understood.

Could you pull up slide 26 of our presentation, please.

So I wanted to respond to the point that full encapsulation and partial encapsulation are nowhere further described in the specification. As I mentioned --

THE COURT: I'm sorry, what slide are we on?

MR. BRAUSA: I'm sorry, we're on slide 26 of our presentation. And this was column 5 from the '651 at lines 30 to 40.

This reference to full encapsulation and partial encapsulation immediately follows the exemplary configurations and characteristics distinguishing between the location. With respect to the kids in the balls, to the extent Your Honor is confused about it, those would be an example of partial encapsulation. They're not inside any of those plastic balls, but they're contained within that relatively disordered mixture. Now, of course, here, we're talking about nucleic acid and not children, but that's just illustrative of what the point and distinction drawn in the specification is.

In terms of both, I don't have a graphic showing it, but obviously it would be a certain percentage fully encapsulated, ideally a high percentage, and then in theory you could have some amount still contained in a disordered lipid mixture. So I think that's what both means in context.

Can you go to slide 50, please.

And, again, this distinction, you heard surplusage being the argument, fully encapsulated is on the left, as explained by Dr. Thompson. Partially encapsulated is on the right. In terms of the unrebutted testimony, certainly, an expert can provide testimony on indefiniteness at a later stage in the case. But there's no reason that an expert couldn't have come forward and said, I disagree with Dr. Thompson's interpretation. I think it's indefinite. But at a minimum, he's wrong. This isn't what the specification was talking about. This isn't how a person of ordinary skill in the art would understand this. This isn't what a person of ordinary skill would take away. And they didn't do that.

Lastly, just briefly on this, the reference to the *Moderna* Court's discussion of encapsulation efficiency. We, of course, agree that the claim term or the claim does not refer to encapsulation efficiency explicitly. The point in raising that consistent with the file history is that during prosecution, both the inventors and the examiner understood full encapsulation to be a proxy for how much full encapsulation there is. So that helps to understand and define the term, which again, is our job here today. And for that reason, we would submit that our construction should be adopted.

THE COURT: All right, appreciate that.

Mr. Klein, what's your response to that? Why not have an expert refute plaintiffs' expert to say we don't agree that that's what a POSA would have interpreted that to be? That has nothing to do with indefiniteness. I mean, isn't that a separate issue that you could have addressed with an expert?

MR. KLEIN: Our position is you go with the intrinsic record. Everything you just heard was attorney argument or extrinsic evidence from their expert.

THE COURT: I just want to be clear, I didn't prevent you, or order that you're not to have an expert to refute their expert's testimony with respect to how they want this term construed. That's a very different position than, well, Your Honor, you punted on indefinite so we didn't get an expert to refute their expert.

MR. KLEIN: I appreciate that, Your Honor. But our position is if you look at the intrinsic record --

THE COURT: Right, that's all you need. I just want to be clear --

MR. KLEIN: That's all you need, yeah.

THE COURT: Okay. That's fair.

All right. Thank you, Mr. Klein.

All right, folks, let's take a ten-minute recess. You can remain seated -- or don't rise for me. But you can get up and stretch your legs and do what you need to do. And I'll be back in ten minutes. Thank you.

(Brief recess taken at 12:52 p.m. until 1:04 p.m.)

THE COURTROOM DEPUTY: Please remain seated.

THE COURT: Wait a few minutes or -- are people still running around or no?

Yeah, let's wait a few minutes. Isn't Mr. Klein missing? I think he wants to hear what -- I like with the Supreme Court when they say: My friend said. We got to start enforcing that in our district court. You know, as you heard my friend say earlier. You know, that's probably the kindest way adversaries have referred to each other. But only before SCOTUS. They never do it in trial court. You wonder why.

I got a new speaker?

MR. PAUNOVICH: A new speaker.

Good afternoon, Your Honor. Joe Paunovich on behalf of the plaintiffs.

THE COURT: Good afternoon, Mr. Paunovich. And you're going to deal with?

MR. PAUNOVICH: What the parties term the mole percentage. There are two of them. They appear in the '359 patent. They're present in all claims of the '359 patent, to be clear. With that, I'll begin.

So this first slide, slide 53, presents both sides' constructions. And the first term that's at issue relates to the mole percentage range for the cationic lipid that's called out in the claim. And the second limitation relates to the

mole percentage range for cholesterol, which is called out in the claim.

For most of this presentation, and for the briefing, you will see both parties focus primarily, if not exclusively, on the mole percentage range for the cationic lipid, and almost to a fault, at that lower end range. That's not to exclude the other boundaries of these limitations, but that's what we'll focus on for purposes of the presentation.

Now, plaintiffs' proposal, to be clear, is that these words, these numerical ranges, can be understood by their plain meaning. And Dr. Thompson provided an opinion from a POSA's perspective of how this intrinsic record and these claim limitations would be interpreted to include conventional rounding.

By contrast, defendants' proposal is to import very precise and exacting limitations that preclude rounding. You can see underlined in red, for the lower bounds of these numerical claim ranges they want to add the words "no less than" and for the upper bounds they want to add the words "no more than". This is not supported by anything in the intrinsic record. And the only extrinsic evidence is the interpretation from Dr. Thompson's view as a person of skill in the art.

So Your Honor may be wondering, why does all this matter? Why are we focused on that 50 percent limitation, that lower bound, for the cationic lipid? And it's pretty

straightforward and simple. Under plaintiffs' construction, if we're looking at the accused products, for example, and they had a cationic lipid mole percentage of 49.5, that would literally infringe if conventional rounding is applied because 49.5 rounds up under conventional, standard, scientific conventions of rounding to 50 percent.

By contrast, under defendants' construction where they would have the Court exclude or prohibit any rounding whatsoever, even if the accused product had 49.999 infinitely, that would not literally infringe because under their construction, again, there would be no rounding allowed. They want an absolute precise and exacting boundary that cannot go any lower.

Now, how does rounding work? Just a brief summary on this. We all learned about it in grade school. We deal with rounding literally every day when we pay sales tax, among any other activities that we go through. And the important point for the Court today as you're thinking about this issue is that when we're talking about rounding, the question or the issue is about what is the significant digit. So the significant digit is going to refer to that last number, that's the number that's subject to the rounding.

So, for example -- and these are out of the context of the claims where we're using 50, because that's the example that the parties are pointing to. If you had 50, and the

significant digit was at the ones place, you would round at the tenths place. Or, in other words, the first number after the decimal point. If the significant digit was at the tenths place, you would round at the hundredths place. If the significant digit was at the hundredths place --

THE COURT: Yep.

MR. PAUNOVICH: -- and so on.

THE COURT: Got it.

MR. PAUNOVICH: That's conventional rounding.

Just to sort of highlight that briefly. I'm not going to dive deeply into the case law, unless Your Honor would like to.

THE COURT: Nope.

MR. PAUNOVICH: The key point is that federal circuit, other courts, when conventional rounding is applied, the issue is the significant digit. There's no precision beyond that significant digit as claimed.

What's that mean in our case? This is a chart that comes right out of Dr. Thompson's declaration, which is at docket entry 84-5, paragraph 8. In yellow, are the two limitations that we're dealing with. And so this is not a matter -- what plaintiffs' proposal is, is not to extend those boundaries beyond what the claim limitations are, but rather to apply that conventional standard of rounding. As you can see here, what that would mean for both the lower and the upper

limits of each of the limitations in the claim.

As Your Honor knows from the briefing, the District of Delaware also dealt with this very same issue for the very same patent, the '359, and adopted plaintiffs' proposal; that is, that the recited mole percentage ranges are understood to encompass their standard variation based on the number of significant digits recited in the claim. And the Delaware Court, as Your Honor knows as well, not an outlier. Not going to go over the cases. There's lots of them, with limited exceptions. And I'll address defendants' arguments that they make about those exceptions. It's very typical for the federal circuit and other courts to apply conventional rounding in the absence of a reason not to.

So what's the intrinsic record here that supports the application of rounding for these claim limitations in this case? I want to start with the specification. And what we see, among other things, but I see in both sides' slides, as well as in the tutorial --

THE COURT: I just want to be clear. This decision by Delaware, you guys like this decision or you don't? I feel like it's like piecemeal. There are times when you guys are relying upon it, and there are times when you're saying, don't listen to them, Judge, I know it's your sister court, but you're not bound by them.

MR. PAUNOVICH: That's a fair question, Your Honor.

THE COURT: So is this kind of like, there are times where you guys you are relying upon them, there are times you're saying we disagree with what this Court has done and we're saying don't follow it?

MR. PAUNOVICH: For this particular term we are relying on the Delaware decision. And there is --

THE COURT: But, Mr. Brausa, just to be clear, there was at least one time in one term you're saying, Judge, neither of us really care about what this Court did, the *Moderna* Court. Am I mistaken about this?

MR. BRAUSA: You're exactly right, Your Honor. I think the key distinction is for the fully encapsulated term.

THE COURT: Right.

MR. BRAUSA: There are reasons we disagree with it. There's also new evidence in the record.

THE COURT: That's fair.

MR. BRAUSA: For this term, there's not new evidence in the record and --

THE COURT: By the way, I'm not saying you can't agree with part of what a Court does and disagree with other parts. I mean, that happens all the time. I just want to be clear that in this case you are asking me, look, we think they got it right, at least with respect to percentages and then how you round up and all the rest of it?

MR. PAUNOVICH: That's correct, Your Honor. And

aside from that new evidence as well, I think the other point that my colleague Mr. Brausa had made is that Pfizer in this case is not advancing that construction that was adopted by the *Moderna* Court.

THE COURT: Yeah, both sides didn't like that part of the decision. Okay. All right.

MR. PAUNOVICH: All right. So stepping back to the specification and why this intrinsic record supports the application of rounding. Table 2 is one of the best illustrations of this. What we see, for example -- so table 2 is a number of different formulations, 16 in total, of the four lipid components of the claim's nucleic acid particles. And those are present in varying mole percentages, right? And what we see, for example, in the turquoise highlighting is -- are examples where the patentee or the inventors chose to identify those mole percentages with a particular precision that goes beyond a whole number. So, for example, the second one, the DLinDMA, that's the cationic lipid, we can see in sample 3 they identified that as being 27.0. For some of the other lipids we see as well where the patentee identified them with a .0 --

THE COURT: I got it. They wouldn't have had a point anything if they weren't intending rounding?

MR. PAUNOVICH: That's exactly right. That's by contrast to sample 1 where we see the use of whole numbers. These would be no different unless the patentee demonstrated an

intent to use significant figures and the application of conventional rounding. And that's what we see Delaware actually, at least in part, relying upon in adopting plaintiffs' construction. Had the inventors intended not to rely on the rules of rounding in significant figures, they wouldn't have had any need to written the whole numbers in table 2 with any trailing zeros.

And I want to point out one that's not highlighted here because it wasn't addressed by Delaware, but I think is particularly illustrative. So that second number we see, sample 1, 40, that's the cationic lipid, 40 mole percent, if we look down at sample 12, we see that same cationic lipid as 40.4 mole percent. Now, if we apply conventional rounding to the sample 1, that would have a different result, for example, if we applied conventional rounding to sample 12 for the cationic lipid. It's just a further illustration that when the inventors desired to identify a numerical value with greater precision and hence apply a different rounding at a different significant digit, they know how to do that and they did that.

Now, the claim language as well is fully consistent with what we see in the specification. Here, and back to those cases from the federal circuit and other district courts, the inquiry is what is the level of precision that the patentee chose to use in the claim's numerical limitations.

We have highlighted in yellow are two claim

limitations that are at issue. And we see that they're claimed as whole numbers without any subsequent decimal places. So the patentee certainly could have claimed 50.0 or 50.00 or 50.0 infinitely. They chose not to do that.

Now, by contrast, we see when they wanted to create a claim with greater precision, highlighted in turquoise, we see for the conjugated lipid, they used the decimal point. 0.5 is the lower bound of the conjugated lipid. This is further evidence that the patentee knew exactly how to claim with greater precision when they wanted to. They did not do that here, as defendants would have the Court read these particular at issue claim limitations.

And as you heard earlier, this is one of those terms where Dr. Thompson has provided an expert opinion. This is part of his declaration at 84-5. He's not purporting to offer a new definition or new interpretation of this numerical claim limitation, but rather, he's doing that hybrid like he did with fully encapsulated. He's looking at the intrinsic record, including the specification, the file history, the claim language, and providing the Court with an opinion of how a person of skill in the art would interpret these claims.

And just like we saw and I just mentioned, what he found is that when the patentees or the inventors wanted to describe mole percentages with more or less precision, they knew how to do that. And a person of skill in the art would

review that record comprehensively, and to understand that they were using significant digits to connote, you know, the application of rounding.

Delaware did rely on Dr. Thompson in his testimony as being supportive of plaintiffs' construction. And the only reason I bring this up is that defendants have known about plaintiffs' reliance on Dr. Thompson, both in the *Moderna* action, and as part of the disclosure process for claim construction in this case. Despite knowing that, we haven't seen them come forward with one scientist from their organizations, one expert to say, you know what, we would look at this, a person of skill in the art would look at this, and we would interpret this --

THE COURT: Differently than Dr. Thompson. I got you.

MR. PAUNOVICH: That's right, that's right. He is the sole testimony on that.

So what are the arguments that are being raised by the defendants? There's four in particular. I want to address each one of those in turn.

The first argument that defendants make is that they say the patentee disclaimed rounding. And the basis for that is they say that the word "about" does not appear before these numerical claim limitations that are at issue in the '359 patent. And where that comes from is actually not the '359

patent itself, but rather, a patent that it is a continuation from. This is the '069 patent, not asserted in this case, but it is related to the '359.

What happened in the '069 is that the initially presented claims, which were similar in many respects, had the word "about" appearing before each of the numerical claim range limitations. What happened next is that the examiner, he rejected the claims over the prior art, and he took issue with the word "about" specifically. And the reason for that is he said, I don't know what that comprising "about" means. To him, it meant that it could be as much as plus or minus 10, 20, or even 30 additional mole percents on top of the claimed ranges.

And I think that's best illustrated, we prepared this graphic in the lower right corner of the slide, to illustrate what the examiner's thinking was when he rejected this particular set of claims over the prior art.

So we see the cationic lipid limitation, 50 to 65 mole percent. And the examiner's saying: Look, when you include the word about in this claim, I'm viewing this as a very expansive, potentially very broad claims here.

So, importantly, if you look throughout that office action, and all of the words that have been cited and quoted and put before Your Honor, there's nothing that the examiner says about rounding. His entire issue is about this very broad scope associated in his mind with the word "about".

So what does the patentee do? To obviate the examiner's concern about that, they removed the word "about" before each of the numerical claim limitations, in response to the examiner's concern. And here again, what do we see in that office action response? Do we see any reference to rounding? No, the patentee doesn't say anything about it. In fact, the patentee also doesn't say or even suggest anywhere in that response that they were interpreting the numerical claim limitations without the word "about" to be a precise number. It's just not there. They removed the word "about" and it -- all that we see within the intrinsic record is that "about" was this really broad range of as much as 30 additional mole percent on top of the claimed ranges.

This is no different as well -- I think the case that's probably most illustrative is the *Copan Italia* case, which is cited in our briefing. In that case, the patentee removed the word "about" from the claim. And the issue was whether or not the number, the numerical range, there it was 90 percent, should -- the defendant said: Well, because you removed the word "about", I want to add the word "precisely", just like that "no less than" or "no more than" that the defendants want to do here. And the Court rejected it. And they said: No, the removal of the word "about" did not mean or compel me to say that this was a precise number that had to be hit exactly on the nose. Rather, I'm going to construe it to

give 90 percent, its full scope, which the Court said expressly would include rounding based on significant digits.

Similarly, this is a bit not exactly on point, but I think it's also illustrative of this point for this Court and in this district is the *Pacira* case. In that case, there was a numerical claim limitation and that numerical claim limitation had the word "about" before it. And what happened was is that the Court said -- the defendant said: We should construe "about" to be limited to the conventional standards of rounding, i.e., with a whole number .5 below or above.

The Court said: No, "about" doesn't mean conventional rounding, "about" means something else. It's something different from conventional rounding. There's conventional rounding and then there's this word "about", and it means something different. That's the *Pacira* case. That's out of the District of New Jersey here.

So what did defendants say? What's their basis? They rely on only a couple cases. There's only a couple cases that actually cited in their brief that deal with numerical rounding, one of which is this *AstraZeneca v. Mylan* case. It's quite distinguishable from the fact pattern that we have here.

So the inventors in that case, the issue was they had repeatedly differentiated between the claimed numerical value, that 0.001 percent weight by weight PVD, from -- they distinguish that from the very number that would be captured by

conventional rounding, 0.0005 percent weight by weight PVD. So we had in that case an absolutely express and clear, unambiguous disclaimer of the very value that would be captured by conventional rounding.

Same thing happened in the *Viskase* case that I think you will hear about, was cited by the defendants. In that case, the numerical claim limitation was .91 grams per centimeter cubed, if I'm not mistaken. And what had happened during prosecution is to overcome to prior art, the patentee had, in fact, added a significant digit in their response to the examiner and said: Our invention is different because .910 grams per centimeter cubed is different from the prior art.

And so in both examples, both the *AstraZeneca* decision as well as the *Viskase* decision, what we found were these clear and unmistakable disclaimers of the actual values that would be captured by the rounding. That's not the situation here.

And for that reason, or consistent with that, the Delaware Court, when it looked at this very same issue, the very same evidence, the very same arguments, found that there was no clear prosecution history disclaimer regarding the rules of rounding. And they declined to accept the defendant's invitation to import these precise limitations into the claim.

And to be super clear on this, because I think you're

going to hear, is rounding a bright line rule or not? We're not suggesting that it's a bright line rule. We're suggesting here or arguing here that the intrinsic record, as well as how a person of skill in the art would view this, is that conventional rounding, as is very typical, unless you have something like an expressed disclaimer, should apply.

Let's talk about the word "about". The *Actelion* decision, to the extent that the suggestion is you don't have the word "about", and therefore, it must not be rounding. Just like the *Pacira* case, we see *Actelion* in the federal circuit, they projected any invitation to create a bright line rule that the lack of approximation language like "about" dictates a precise value.

All right. So what's the second argument raised by defendants? They make this argument, actually, I believe for the first time in their response brief, that the 50 percent mole percentage limitation for cationic lipid is some sort of critical minimum, or that otherwise, you know, was stated as being the only limitation where you might get some unexpected results. That's not true.

What we look at -- what we can see when we look at the portions of the specification that are cited by the defendants is that all that's disclosed is that the lower bound of the cationic lipid, that they point to these references where it said about 50 percent as a lower bound. It doesn't

say it's a critical minimum. We don't see anything saying that, in fact, that you can only get the benefits of this invention if it's at 50 mole percent. It's simply a broad and general disclosure. And it certainly doesn't say anything about rounding, or that 50 mole percent should exclude values that are captured by it, like 49.5. percent. I'll address that on a later argument from defendants.

Even in -- actually, I want to go back just briefly. In the tutorial slide, slide 34 from defendants, they also point to, and I think you're going to hear argument about, well, there were unexpected advantages associated with 50 mole percent cationic lipid. And I think we saw or we're going to see some slides from them on this very term. And they cite to and point to a portion of the specification where there is some discussion about some surprising results associated with this invention, but -- and all that they highlight is the range for the cationic lipid. What they don't highlight are all the other lipids and their ranges that are associated with the overall invention. This invention is not just a cationic lipid. There are four lipids that are part of it and there are ranges associated with all of those. And absent from any of the portions that they're going to point you to or anything else in the intrinsic record is a statement from the patentee saying: My invention is dependent wholly, or even partially, on the cationic lipid being at an absolute minimum, or critical

minimum as they term it, you certainly won't see those terms, for the cationic lipid.

We also know that the patentee contemplated that the cationic lipid could be below 50 percent. And we see that from two different sources.

I'm going to go back here.

So, for example, in the '359 patent at column 20, lines 33 through 39, we see a disclosure about the non-cationic lipid. And what's important about this is that it says that non-cationic lipid can be up to 60 mole percent of the total lipid present in the particle. Remember in the tutorial, the mole percentages, they all have to add up to a hundred. It's four lipids, and the combination of those, the mole percentages, they all add up to a hundred.

So what do we know by implication? If the patentee contemplated that the non-cationic component of the invention could be as high as 60 mole percent, then the cationic lipid absolutely was contemplated by the patentee as being potentially less than 50 mole percent.

We also see from table 2, that table 2 we looked at earlier from the specification -- could we go back to that? I think it's slide 60.

So we look at some examples. And these are non-limiting examples. Before the examples begin in the specification, the patentee is very clear in saying these are

examples, they're illustrative, they're not intended to be limiting. But for example 2, table 2, we see some of these exemplary formulations of the lipids that comprise the lipid nanoparticles that are at issue in this case. Remember that second column, which is DLinDMA, that's the cationic lipid, what did we see? We see exemplary formulations of cationic lipid that are below 50 mole percent.

So, respectfully, we think it's abundantly clear from the specification that there is no stated critical minimum. In fact, there's evidence that the patentee contemplated formulations that would have cationic lipid below that 50 mole percent that's in the claim limitation.

Can we go back to slide 55 now, please?

So defendants' third argument. They say 50 mole percent for cationic lipid was distinguished over 49.5 mole percent. They're making this argument to try to line up the case with *AstraZeneca* and with the *Viskase* case. But that's not actually what the intrinsic record shows.

So what do they point to? They point to the single portion of the specification, although it gets repeated similarly in other places. They say, well, there's a dividing line, and if you differentiated 50 percent from 49.5 percent. That's not the case. We have highlighted in yellow, element B of this exemplary formulation and it says: Cationic lipids comprising from about 50 mole percent up to 85 mole percent.

That's one disclosure for the cationic lipid. Element C, one or more non-cationic lipids comprising from about 13 to about 49.5 percent. There's no distinction drawn between 50 and 49.5 cationic lipid. In fact, there's not even a comparison or differentiation between the cationic and the non-cationic. These are two different disclosures about different lipids that comprised the claim invention.

And, in fact, although defendants say that the Delaware Court didn't have this 49.5 mole percentage argument before it, and we'd acknowledge maybe it's raised in a slightly different manner here by Pfizer, Delaware Court actually looked at this disclosure of 49.5 percent non-cationic lipid, and they found that that was yet another piece of intrinsic evidence that supported the Court's adoption of the plaintiffs' construction, and illustrated that the inventors knew how to and did use significant digits consistent with the application of conventional rounding.

Which brings us to the fourth argument raised by defendants, which is a new argument here that wasn't raised in Delaware, but we don't think is -- there's no new evidence regarding this. This is simply, their argument in short is that the word "from" appears before the numerical claim limitations that are at issue in this case. And they say: Well, that word "from" is a word of precision, an exacting word that indicates a precise point and you shouldn't apply

rounding. There's no support for this argument either.

What defendants point to are a variety of cases, including the *Esco*, *Printeron*, and *Inland Diamond* case. I think what's notable about those is none of these cases actually involved a numerical claim limitation. Rather, each of those cases dealt with the issue of the application or the interpretation of the word "from" as it relates to some directional dimension of a tangible device. They literally did not construe "from" relative to a numerical claim limitation.

And I think what's notable, so, for example, the *Esco* decision, the claim term at issue was an inward projection in the front end axially extending from the front thrust service. And what's notable about that case is that the *Esco* decision didn't, in fact, construe the word "from" to mean that that's a precise point or an exacting point that you can't cross in any way. Rather, they said, and this is a direct quote from that decision: The term extending from will be construed to mean starting from or immediately adjacent to.

And so we see, even in the primary case the defendants cite to for this new "from" argument, that the Court was very clear in a non-numerical context that "from" doesn't mean exactly at that point. It can actually also capture things that are immediately adjacent to, just like numerical rounding does.

So this shows that even in a non-numerical context,

but certainly in a numerical context, that "from" doesn't have the meaning that defendants would like to import to it.

With that, Your Honor, for all those reasons, we would respectfully ask that you adopt plaintiffs' construction for this term. And I will reserve any remaining time to address the defendants' arguments.

THE COURT: All right. Thank you, Counsel.

Sorry, Mr. Klein, go ahead. By the way, is there a case that does involve the interpretation of "from" when it's connected to a numerical claim, like what -- I'm sorry, is it Mr. Paunovich? Is that the right name?

MR. BRAUSA: You're correct, Your Honor.

THE COURT: Okay. That's what he's claiming, that these cases you're citing to really don't deal with numerical claims, they're kind of -- you know, they're not analogous. So is there a case that you can cite to and say, no, Judge, this is exactly on point with what we're talking about here?

MR. KLEIN: We don't have a case that uses "from" right before a numerical --

THE COURT: We don't, okay.

MR. KLEIN: I'll get to "from". I still think that's a relevant argument because "from" is a claim term and you have to give it some meaning.

THE COURT: I'm not necessarily disagreeing. I just want to know, am I missing a case or is there a case that you

can point to, either side, that says, no, here's a case, this Court has interpreted "from" right preceding a numerical claim, and that's on point for this Court to at least consider. But that's not out there?

MR. KLEIN: No. I didn't see it going the other way, either.

THE COURT: Okay, that's fair.

MR. KLEIN: So as I have done with the other terms, Your Honor, I tried to focus on the core dispute. And obviously, the core dispute is basically whether from 50 mole percent means exactly 50, or rounding applies and it includes 49.5.

We have five points to make. And I'll do it fairly quickly. The first point, which I believe is undisputed, I think I just heard this, there is no bright line rule that presumes rounding. So we're applying the general claim construction principles to this question. And we do rely on the *AstraZeneca* case. And the *AstraZeneca* case stands for the proposition that you don't round if it leads to an acontextual construction. So this is kind of a classic legal claim construction dispute. You look at the claim term, the range, whether rounding makes sense in view of the intrinsic record. That's our position.

So turning to the intrinsic record. The record shows that 50 mole percent meant exactly 50, and, in fact, is

different from 49.5. In the *Viskase* case, the Court talked about whether a boundary was set in the intrinsic record. And when a boundary is set that distinguishes measurements, that's a basis not to apply rounding. We submit, that's what we have here.

And on slide 34, this was mentioned by counsel earlier, we rely on the '359 patent, column 3, lines 18 to 28, that talks about one aspect of the present invention. And it talks about how you can have cationic lipids from about 50 mole percent to 85 mole percent. And then two lines later it uses 49.5. The inventors knew how to say 49.5 when they meant 49.5. And then two lines after that, the 49 -- just to be clear, the 50 mole percent is for the cationic lipid component. Then they say 49.5 percent for the non-cationic lipids, those are cholesterol and the phospholipid. And then two lines after that, they talk about these conjugated lipids, I don't know if it talks about conjugated lipids, those are the PEG lipids. And then it says from about 0.5 mole percent.

Now, as counsel said a number of times, the mole percentages need to add up to 100. And that's what you have here. You have 50 mole percent, plus 49.5, plus 0.5. That was done on purpose by the patentee because it adds up to a hundred. And so there's a clear distinction in the specification between 49.5 mole percent and 50 mole percent. But plaintiffs' position is that 49.5 is the same thing as 50.

They're equivalent. There is no difference between the two once you apply rounding. The inventors, and the patentee, thought differently.

And this isn't the only part of the spec that distinguishes between 50 and 49.5. If we go to slide 35, they do it again in column 5. They do the same type of analysis, 50, plus 49.5, plus .5. If you start applying rounding to this, it doesn't get you to a hundred, it doesn't work.

And we have seen also a cite on this slide, slide 35, where this concept distinguishing between 49.5 and 50 is again repeated in column 14. So over and over again the inventors use 49.5 when they meant 49.5, and 50 when they meant 50.

So where did the 50 come from? You heard a little bit about this during the tutorial, and I'm not going to walk through this complicated slide again. But, in essence, the data in this specification led the inventors to conclude that 57 percent of -- molar percent of cationic lipid was among the most potent inhibitors. And then if you got below 57, you still had potency, but it wasn't as potent as the 57. And so the inventors decided to draw a boundary at 50. And we see that -- I'm going to slide 37 -- in the '359 patent, column 19, lines 13 to 18, the inventors then say the cationic lipid may contain at least about 50 and above. Now, you can ignore the about because that obviously was struck during the prosecution. But the point here is that the inventors, when they wrote this

specification, set a boundary for the cationic lipid mole percent, and that boundary to get the unexpected results were 50. And I'll get to that in a second.

Also, the intrinsic record never describes unexpected results below 50 mole percent. They obviously knew how to say 49.5, but they never said use -- if you use 49.5 mole percent of cationic lipid, you can achieve the unexpected results that they purportedly achieved and recited in the patent.

So now we get to the claim language. And the claim language obviously says from 50 mole percent. And this makes a lot more sense when -- now that we have gone through the specification and seen how the inventors distinguish 49.5 and 50. And we cited the *Esco* case. This is Judge Bryson, who's obviously a federal circuit judge sitting by designation. And we have a nice colorful example. That under the plain and ordinary meaning of "from" -- and it's a claim term -- it would not be proper to say, for example, someone is traveling from the courthouse to his office when that person actually begins his journey three blocks away from the courthouse.

If you look at the claim -- let me go back to the claim -- on slide 40, the claim term is a cationic lipid comprising from 50 mole percent to 65 mole percent. You don't need "from". You don't need "from" there. They could have said a cationic lipid comprising 50 to 65 mole percent. So "from" has to have some meaning. And this is what I alluded to

earlier. Plaintiffs are ignoring "from". They're giving no meaning. Once again, surplusage is supposed to be avoided in claim construction. And so you apply this concept of "from". I know the Court didn't address "from" before a range, but he said there's a plain and ordinary meaning of the term "from". And it's a claim term here so it should be applied.

The prosecution history also relies on the term "from" 50 mole percent. And it's clear, when you look at the prosecution history -- I'm on slide 42 -- that the alleged new, unexpected, and surprising results were tied to formulations with increased amounts of cationic lipid, one or more cationic lipids comprising from 50 mole percent to 65 mole percent. And the applicant said that's what's providing the unexpected and superior advantages, it's not the non-cationic lipids, it's not the PEG lipid, it's having from 50 mole percent of cationic lipid. So this was a boundary that was set not only in the intrinsic record, but also in the prosecution history.

And now to address plaintiff's primary arguments. So they rely on the table 2. They use a different -- we're quoting a brief, they put table 2 up there and state that, look, if look at table 2, you see numbers like 40 in one instance, 60.0 in another, and there's no reason to do that other than to convey that the latter has more significant digits for rounding purposes. That's an attorney argument, Your Honor. And at deposition, Dr. Thompson was asked: Do you

know why it is that the inventors use varying numbers of significant figures in the table 2, sometimes using trailing zeros, and sometimes not?

And he said: I don't know why. Could be something as simple as the more sensitive balance was out of service.

This, by the way, was not before the *Moderna* Court. So there is new evidence in front of Your Honor that was not before the *Moderna* Court.

And so plaintiffs' own expert didn't support plaintiffs' theory that if you use some numbers of a particular significant digit and others with a significant digit, that it has some meaning.

THE COURT: Mr. Klein, does this change your position? Or are you asking me, look, the intrinsic record is what should govern here, but to the extent I am going to consider plaintiffs' expert, then I should consider this? Is that the argument?

MR. KLEIN: Yes, Your Honor.

THE COURT: Or are you saying: No, no, we want you to consider Dr. Thompson's testimony? I don't know if that's the ask or the ask is, don't consider it at all, but if you're going to consider it, then make sure you're looking at this?

MR. KLEIN: It's the latter, Your Honor. Our position is you look at the -- if you want to know if 49.5 rounds to 50, you look to see if there's a distinction between

49.5 and 50 in the specification. And that's what happened in the *AstraZeneca* case. And there is. There is a distinction between 49.5 and 50. So the fact that there's a table that says -- I forget -- 40 and 60.0, that doesn't matter. And their own experts say he doesn't know why they did it.

So you can't read too much into this table 2 that doesn't talk about 49.5 versus 50. You should look at the portions of the spec that actually distinguish between the two figures that are at issue in this dispute.

And, finally, Your Honor, the *Moderna* case, just to be clear, the *Moderna* decision relied primarily on the concept of prosecution history disclaimer, which -- and said that striking "about" during prosecution doesn't necessarily mean rounding is inappropriate. That's basically what the *Moderna* Court said. But the *Moderna* Court did not address the specific arguments that we're making here with regard to the specification distinguishing between 49.5 and 50. The *Moderna* Court, I think counsel admitted, didn't address the claim term "from". And, of course, the record was a little different because they didn't have that testimony from Dr. Thompson.

THE COURT: All right. Thank you, Mr. Klein.

MR. PAUNOVICH: May I have two minutes, Your Honor?

THE COURT: You may.

MR. PAUNOVICH: I want to address briefly just a couple arguments. Your Honor, the first was, again, this

argument about was there a distinction between 50 and 49.5 percent cationic lipid. And what I heard defendants to say is that while the patentee, they obviously knew how to use the words 49.5, and so, you know, if that's what they really meant by 50, they should have done it here. But that misses the point. The conventional -- you don't need to say what the standard scientific convention of rounding covers. It's something that's understood by people of skill in the art and that is typically applied absent some circumstance like a disclaimer, which isn't present here.

If the patentee had chose to use 49.5 mole percent as a lower bound for cationic lipid, then the application of conventional rounding would be different than 50 as a whole number. Instead of being .5 below or above for that lower bound, if it were 49.5, since we have an additional significant digit, their rounding would be applied at that hundredths place. So we would have 49.45 up to 49.54.

And that's the entire point here in how courts, when they look at rounding, and when rounding applies, the question is what's the significant digit, and you apply the rounding on the basis of that. So the fact that the patentee for a different lipid said: Well, I'm going to describe that upper bound as 49.5, is entirely irrelevant to the issue here, which is, we've got a claim limitation that has 50 mole percent as a whole number with no trailing zeros for cationic lipid.

Conventional rounding tells us what that literally covers.

Second point I want to address, table 2, and their argument that, well, you know, look at -- this is, I think, their slide 36, the one that we saw here, it's got this fancy graph. And what it is is it was looking at those exemplary formulations of all four lipids. And as you can see from table 2, cationic is not the only one that changes. All the lipid mole percentages change and vary. So there's no control for what's happening in terms of potency relative to the cationic lipid mole percentage. Rather, these are just sort of disparate formulations that are disclosed. So we don't know, we can't draw any conclusions about the potency associated with cationic lipid.

But I think what's interesting to note is the defendants' argument, they said: Well, look, if you compare sample 9 that has 57.1 mole percent cationic lipid, and you compare that to samples 10 and 12, which have a lower cationic mole percentage, at least this disclosed example, which is non-limiting, they were less potent. However -- and so they're suggesting that as you go down, you're not receiving the benefits of the invention.

But if we look in the very next row, samples 11 and 12, we have cationic mole percentages of 42.6 and 40.4, respectively. And we see the potency associated with those exemplary formulations is actually better than, for example,

sample 12 -- sample 13. That's not surprising. Again, as I just mentioned, if we look at the overall four lipid components, they're all varying. So this wasn't an experiment to test and assess and control for what happens when I raise or lower this cationic mole percentage. Rather, it's simply an assessment of these different formulations. And, respectfully, I don't think any conclusions can be drawn from that.

Third argument -- or the last argument is about Dr. Thompson. And they say: Well, we got -- there's something different from *Moderna*, we got this testimony from him when he was asked at deposition, you know, why in table 2 did the inventors add these trailing zeros in some instances and not others. And unremarkably, he said: I don't know. He wasn't in the lab. He didn't talk with the inventors and ask them why did you do this. That's not the point. In fact, it misses the entire point. The point is, how would a person of skill in the art interpret this intrinsic record? The fact that the inventors in this case wrote this application to include those trailing zeros.

And, again, not surprisingly, like many courts and persons of skill in the art would look at this, it's a reflection of them understanding how to use significant digits to indicate greater precision when they wanted to. So he doesn't need to know why they chose for those exemplary samples to use a trailing zero or not. What it reflects is a choice in

some instances and not others to use trailing zeros. And that's consistent with the use of significant digits and the application of rounding.

THE COURT: All right. Thank you, Counsel.

We got one more, don't we?

MR. NIMROD: We do. Last one.

THE COURT: I'm going to ask you guys to keep it moving. Mr. Klein's probably going to enter a triathlon after today. He's on his own over there. Nobody wants to tag in for him. He's going to lose his voice.

But I will tell you, though, folks, I do appreciate your efforts today. I know this is a little bit of a marathon, and this is just the way I run things, but it has been absolutely helpful from both sides. So I always encourage folks to come -- that work in here, in the courthouse, to come into these hearings because the patent bar is exceptional and you guys fit the bill on both ends from plaintiffs' counsel and defense. So let me thank you in advance so that when we're done today I can adjourn and get you out of here. But I did want to say that on the record that I am always impressed and these hearings are unbelievably helpful to the Court. We are not experts in this science. This is not an area of expertise or an area that I practiced in before I joined the bench years ago. And I always find these hearings educational and helpful. So I thank both plaintiffs' counsel and defense, on both sides,

you have a lot of information for me to consider.

And with that, Counsel, I'm going to let you come back and talk to me about "consisting essentially of", is that where we are?

MR. NIMROD: Thank you, Your Honor. Yes, we are. Ray Nimrod again, Your Honor.

The "consisting essentially of" claim term is only in the '378 patent claims. It's a transition term, as we call it, at the end of the preamble, before the body of the claim. And there are generally three types of transition claim terms. One is open, such as the word comprising. So if you say comprising a mixture of X and Y, and you have an unlisted ingredient like Z, then it's covered if you got X and Y with Z. Because it says comprising, you can have additional unrecited elements.

The second type is a closed claim term. For example, a mixture consisting of X and Y. In that situation, a mixture of X, Y and Z, where Z is unrecited, would not be covered by the claim because it's closed.

"Consisting essentially of" is the one in between, it's partially open. You say a mixture consisting essentially of X and Y, then a mixture of X, Y and Z would be covered if the material Z does not materially affect the basic and novel properties of the mixture. If it does, then it is not covered.

Now, the parties have no dispute as to what the words "consisting essentially of" mean, the plain meaning of those

words in the law. And the federal circuit has explained that "consisting essentially of", transition term, permits inclusion of unlisted components as long as they do not materially affect the basic and novel properties. So the parties' dispute is what are the basic and novel properties for the '378 patent claim.

As we show here, the plaintiffs' proposal is that the basic and novel properties of the claimed invention of the '378 patent are the combination and concentration of lipid components. In contrast, defendants say that the basic and novel properties are increased activity, improved tolerability, significant increase in therapeutic index, and stable, compared to lipid particles having less than 50 percent cationic lipid.

Now, why are they proposing that? For two reasons. One is, they want to create a non-infringement defense to say that these claims don't cover formulations with less than 50 percent cationic lipid. And they also want to create an indefiniteness argument. They want the Court to say, well, these are the basic and novel properties, and guess what? The patent doesn't describe the proper tests and how to run them to determine if you have them.

As I'll explain, the Court should reject the defendants' construction and adopt the plaintiffs' as being consistent with the law. Just very briefly, what is the law? Well, you're looking to see what the basic and novel properties

are, if you know the content of novelty, Your Honor, it's how you distinguish things from the prior art. And you can look in two places generally to see how the claimed invention was distinguished from the prior art. One would be the specification, and that's shown in the *AK Steel* case. And you also can look to the prosecution history if that is what reveals how the invention was distinguished from the prior art. And it's shown in the *L'Oréal* and *Aventis* case.

So the starting point, of course, for any kind of analysis as to the basic and novel properties is what is the invention at issue here. And this is obviously very important, Your Honor, because the claimed invention here, as we see, is a nucleic acid lipid particle that has a cationic lipid limitation with no numerical limitation there. So that is the invention of the '378 patent. It also has a limitation where it requires or allows for a mixture of what we call the non-cationic lipids, phospholipid and cholesterol, going from 30 to 55 mole percent. And what does that mean? That means that, of course, that the cationic lipid can be less than 50 percent, because otherwise, you couldn't have 55 percent of those two.

So now the question we then ask ourselves is, all right, well, how was this invention distinguished from the prior art? Not the invention of some other patents, but how is this invention distinguished from the prior art? And, Your

Honor, we could turn to the prosecution history.

In the prosecution history, the examiner cited several references against this claim when it was pending. And one was the Li reference. And did the applicant distinguish it based on the four alleged improvements? Did the applicant distinguish it based on a comparison of 50 percent or less? No. The applicant distinguished it based on the four-component lipid system and the recited concentrations that were in the '378 patent claims. You see right here in the slide, Li is silent on RNA delivery by a lipid particle containing a cationic lipid with phospholipid, cholesterol, and PEG lipid, the four lipids that are listed in the claim. And they say: As such, Li provides no disclosure of the four-component lipid system as claimed, or the recited concentrations of the lipid components. Again, the recited concentrations are for the phospholipid, cholesterol, and the PEG, nothing is recited for cationic. So the patentee didn't come in and say: Well, look, we have a 50 percent limit on cationic. No. They relied on the claims features that are set forth in the '378 patent.

And there's other examples as well. They said the examiner cited several references, one was Semple. How was it disclosed? They said Semple discloses a two-component lipid system and does not teach or suggest particles with a four-component lipid system as claimed. They go on and say Semple teaches away from the claimed phospholipid/cholesterol

concentrations and molar ratios, that's the 30 to 55 percent mixture, and also distinguishes based on the 30 to 15 recited limitations in the claim. And they summed it up by stating that all the prior we looked at -- the Patent Office looked at, failed because of these three reasons, all of which are claim limitations. A four-component lipid system, a cationic lipid having a protonatable tertiary amine, or RNA delivery using a lipid particle containing a cationic lipid, a phospholipid, cholesterol, and PEG lipid, at the recited concentrations.

And that is the basis for plaintiffs' construction because the case law says you look to see how the claimed invention was distinguished over the prior art. And we see here very explicitly in the prosecution history how the invention at issue here was distinguished over the prior art.

Now, the defendants criticized plaintiffs' construction in a couple ways. One, they say: Well, you're turning this claim into a comprising claim. Well, we're not doing that. An example would be that if you had a particle that had five lipids, and you had like the five lipids present in your comprising claim, the presence of the five lipids would not preclude coverage because comprising would allow the fifth lipid as long as you met all the limitations.

But separate from that, that would not be the case with consisting essentially of, as it should be construed here. It was very clear that the applicants here said ours is a

four-component system. So the consisting essentially of, based on the basic and novel properties, which is the combination and concentration of lipid components, would not cover a particle with a fifth lipid.

The second argument they make against our construction is, they say that, well, you can't say that the combination and concentrations of a lipid can be the basic and novel properties because those are claim elements. But that's not what the law is, Your Honor. The question is, how were the claims distinguished over the prior art? And in some cases, people rely on some advantages and say: Well, I got these advantages that are unexpected here.

That's not how these claims are distinguished, and that's perfectly fine to rely on claim elements. For example, in the *Aventis* case that we cite, Your Honor, that says all of the asserted claims required that docetaxel be dissolved in polysorbate 80. So the claim expressly recited polysorbate 80. And the Court concluded that because the applicant in that case had distinguished the prior art on the basis of polysorbate 80 being the one and only surfactant, that recited claim element was the basic and novel property, and you couldn't have a second surfactant.

The same is true with the *L'Oréal* case, where the claims explicitly recited stabilizing avobenzone by adding specified amounts of octocrylene. That's how it was

distinguished, the Court said: The basic and novel property, stabilizing avobenzone with respect to UV radiation by adding a specified amount of octocrylene. All claim elements, but that's because that's what the records show. The issue is, how did you distinguish the claimed invention?

So, Your Honor, for the claimed invention here, which has no cationic lipid limitation, and also has a non-cationic lipid limitation that goes from 30 to 55 percent, defendants do not cite a single part of the specification or file history where that claimed invention was distinguished based on these four advantages that they're talking about, or based on having less than 50 percent.

So what did they do then? They take a different tactic. They went to change the invention that's at issue before Your Honor, the '378 patent. They want to read in a 50 percent limitation into the claims of the '378 patent, so they can make it like other patents in the family, the molar composition, or lipid composition family, that have a 50 percent lipid. So they say in their proposal for the basic and novel properties that those properties have increased activity, improved tolerability, significant increase in therapeutic index, and stable, compared to lipid particles having less than 50 percent cationic lipid. And they concede what that means is we're reading in a limitation in the '378 claims, and they have to have no less than 50 percent cationic

lipid. On page 29 of their opening brief they say: The basic and novel properties of the claims of the '378 patent must be interpreted to permit no less than 50 percent cationic lipid.

So that is the impact of what they're asking for with their construction. The Court should reject it because there is no limitation in the '378 claims to a 50 percent cationic lipid.

Let's look at the basic straightforward analysis, Your Honor. Are the claims limited in that way? Well, starting with the claim language, which is what you always do with, obviously, claim instruction, we see that claim 1 of the '378 patent, unlike other patents in that same family, does not recite a cationic lipid limitation. So the claim language says, no, there's no 50 percent lower limit.

And then we go on. And you can compare that claim in the '378 to other patents in that lipid composition family like the '359 patent, claim 1, that you heard about earlier in connection with the rounding issue. That one does have a limitation of a cationic lipid comprising 50 to 65 mole percent of the total lipid present in the particle. That was the invention of a '359 patent, claim 1. It is directed to a preferred embodiment that's set forth in the claim. A preferred embodiment, Your Honor, that simply means something that the applicant believes to be preferred in some manner. But preferred embodiments are not limiting. They're only

limiting if you, in fact, write the claim in a way that only covers the preferred embodiment. They're simply examples.

So the '359 patent, claim 1, along with the other three below it, those are inventions that are directed to particles that have a lower limit of 50 mole percent of the cationic lipid. But that is not recited in the '378 patent claims.

And, Your Honor, now turning to the Delaware decision. In that case, the defendant attempted to read in a 50 percent lower limit to the claims in the '378 patent, and the Court rejected that attempt. And we agree with the district court in that situation.

The Court noted that: Towards that, I, again, first turn to the claim language itself. All of the earlier issued patents in the molar ratio patent family specified an express cationic lipid mole percent limitation. As we just looked at. By contrast, claim 1 of the '378 patent, and the numerous dependent claims, do not set forth a cationic mole percent limitation, but do recite explicit mole limitations related to other lipid elements. Thus, the plaintiffs knew how to include lipid mole percent limitations and chose not to do so for the cationic lipid component of the claims of the '378 patent. And the Court goes on and says: Unless otherwise compelled, a claim term should be construed consistently across related patents, but this proposition does not permit importing terms

or limitations into the claims of related patents that do not recite the disputed term.

And that is the situation here. There is no 50 percent limit in the '378 claim, and none should be read in.

Now, the defendants, with their proposal where they're trying to take "consisting essentially of" to basically rewrite the claims have -- there's a second flaw in that. Not only are they going to -- they're trying to read in the limitation, they're also rewriting another limitation of the claim, and that is the limitation to the mixture of phospholipid and cholesterol from about 30 to 50 mole percent. That's an explicit limitation in claim 1 of the '378 patent claims, but according to defendant, the cationic lipid has to be at least 50 percent. Well, if the cationic lipid is at least 50 percent, Your Honor, then what does that mean? That means that the claim element 1(c), which says 30 to 55, it has to be written to 30 to 50, because if you have to have at least 50 percent cationic, then you can't have above 50 of the non-cationic, Your Honor.

So what their construction is doing is including -- excluding embodiments that are explicitly claimed in claim 1, and say: No, you can't have 50 to 55 percent, we're going to rewrite that limitation. It's impossible to then practice the full range of the claim as they are explicitly written. So they want Your Honor to basically rewrite two elements of the

claim, add a number here, at least 50, strike this 55, make that one 50.

Now, Your Honor, the District Court of Delaware relied on that change as well to say: No, I'm not going to write in a 50 percent lower limit to the claim. The Court said: If that mixture is at the high end of the claim range, that's the mixture of the phospho and cholesterol, then the mole percent of the cationic lipid in that same nucleic acid lipid particle cannot possibly be a least 50 percent. Accordingly, applying *Moderna's* construction would render another part of the claim language invalid.

I just want to pause here for a moment, Your Honor. There's been a lot of discussion today about some parts of the specification that relate to embodiments, preferred embodiments, that have at least 50 percent, and also have non-cationic going up to 49.5. But those are simply some preferred embodiments. Other preferred embodiments don't have those limitations. That's the embodiments that are at issue here today. So in the specification it talks about, in some embodiments, the non-cationic lipids, e.g., one or more of the phospholipids, or cholesterol, may comprise from about 30 to 55 mole percent. So the patent specification does describe some preferred embodiments that are limited to 49.5, but that's not claim 1 of the '378 patent, and that's the invention at issue here. Your Honor, the important point is to decide how is that

invention distinguished from the prior art? And it talks about there are other embodiments. And it distinguishes between the two where the non-cationic is from 13 to 49.5. But you ask yourself, is that the claim at issue here for the '378? The answer is no.

And then in conclusion, the District Court in Delaware decided that *Moderna's* proposed construction, that the cationic lipid in the nucleic acid lipid particles must have at least 50 percent -- mole percent, absent from the claim language, and is not present in the specification description of the invention. To import that limitation from the preferred embodiments in the specification would run counter to well-established federal circuit law. And that's what they're trying to do here, both in two respects, Your Honor. They're trying to say, well, take that 50 percent from a preferred embodiment that's not applicable to this claim, read it in, and then look to the specification and see what the patent says about that preferred embodiment which is not at issue here.

And now, Your Honor, there could be no doubt that the only way, their only justification for saying that you should rely on these four advantages, is based on the discussion of the preferred embodiment having at least 50 percent cationic lipid and a phospholipid/cholesterol combination limited to 49.5. In their opening brief they say: Here, the '378 patent explains that the present invention, in quotes, comprises from

about 50 mole percent cationic lipid, is what achieved the surprising discovery that such formulations have advantages over the prior art. And they cite the '378 patent at column 6, lines 6 to 13. And you go there, that is a discussion of a preferred embodiment that has at least 50 percent, and has the phospholipid/cholesterol combination of 13 to 49.5. But that is simply one example. And nowhere, nowhere in the intrinsic evidence do you see the applicant ever distinguish the invention of '378, which does not have these limitations on the basis of these alleged advantages.

And I think the *L'Oréal* case is instructive on this point, Your Honor. In that case, the '378 patent and '359 come from the same original patent filing, but there are continuations down the path. And, of course, continuation issued patents need to be directed to different inventions. That's the whole point of getting multiple patents on it. So one might be directed to preferred embodiment A, another one to preferred embodiment B. But what is said about preferred embodiment A to distinguish the prior art is not applicable to B unless you say it's applicable to B. In the *L'Oréal* case, the defendant there tried to take something that was said about one of the patents in the family, separate from the one at issue, and say: Well, that's what you should say are the basic and novel properties. But the Court said: No, the '354 patent and the '150 patent are children of the same parent patent

application, and therefore share the same specification. The Court must be careful not to attribute properties of the '150 patent, which specifically claims cosmetic screening compositions for the protection of human dermatitis -- epidermis, excuse me, to the '354 patent.

Similarly here, the defendants are trying to have the Court take advantages that are ascribed to the preferred embodiment to having at least 50, and say: Well, I want you to apply that in the '378 patent claim. But the question to ask yourself again is, well, how was this patent distinguished over the prior art? The way it was distinguished over the prior art was what we saw with respect to Li, Semple, and the other prior art. It was based on the four-lipid system at the recited concentrations and nothing else.

Now, kind of recognizing the error of saying that you should read in this limitation they, in their response brief, they kind of walk it back a bit and they say: Well, maybe you don't have to worry about the comparison to 50 mole percent. But they say: Regardless of how the point of comparison is characterized. At the very least Your Honor should say that the basic and novel properties over the prior art are increased activity, improved tolerability, increase in therapeutic index, and stability. There's two problems with that. One is, as you see, they're still relying on column 6, starting at line 6, that is to a preferred embodiment that is not at issue in this

case with respect to the claimed invention. It goes on and talks about examples. And they said they're not -- these are just illustrative examples. Nothing in there about how one would distinguish the embodiment we saw earlier that has 30 to 55 percent of a structural lipid. So that's problem number one, they're still trying to go to the specification part that's talking about a different invention and say: Well, just ignore that, but just pretend we didn't look at it anyway.

And the second reason is, if you take this compared out, what's it mean? Compared to what? Increased activity. Compared to what? Improved. As compared to what? The linchpin of their construction was that you have to have improvements over having less than 50 percent. And as we just saw on the chart that Mr. Paunovich showed you, Your Honor, that they put up and they highlighted three of the five, they said: Well, the bottom's the best and it gets better as you go down. Two of the ones that are in the middle there had less than 50 percent.

So there was never a time in the, at any point, intrinsic evidence where the invention at issue here was distinguished on the basis that the applicants are proposing. We know what they were distinguished on. They were distinguished based on the claim elements that are highlighted here on the left-hand side, and on the right-hand side, four components, cationic lipid, and that recited concentrations,

and nothing more.

THE COURT: Thank you, Mr. Nimrod.

Mr. Klein.

By the way, do we need a break?

Nobody? Okay. Then let's go. I wasn't asking for me, I'm asking for you all. I'm ready to go the next five hours. You guys want to add some more terms, let's do it.

MR. KLEIN: I only have about four and a half, so I think we are --

THE COURT: I'll take it.

Just bear with me, I just want to make sure I have the right slides.

Okay, I'm ready.

MR. KLEIN: Okay. Thank you, Your Honor.

We're on slide 50. Again, the term we'll talk about is "consisting essentially of", and we'll talk about the '378 patent.

Before I get into the construction part, Your Honor, I want to give you some context for how we got to this patent. And you saw this timeline during the tutorial, but I'm going to unpack it a little bit.

Priority date here is 2008, so quite some time ago. There are two patents in this family, the '359 was filed in October 2011 and issued in July 2013, obviously, long before the pandemic. And then Comirnaty, the COVID vaccine was

approved in December of 2020. And then on April 9, 2021, there was a disclosure of the molar ratio in defendants' product. Three days later, plaintiffs filed the application that led to the '378 patent, which issued in October 2021.

Now, if we go to the next slide, this is the April 9th, 2021, disclosure. And the disclosure was that the cationic lipid molar ratio in defendants' product is 46 percent. Okay. So this was disclosed on April 9th, 2021. And then on three days later, plaintiffs literally ran to the Patent Office in just three days to get a new claim. Why? Because the '359 patent has a limitation requiring from 50 to 65 mole percent, which we talked about. But they learned three days earlier that the defendants' product is only 46 mole percent, so they took it out. They took it out of the claim and they added the "consisting essentially of" term. And instead of having a molar percentage range for cationic lipid, they say a cationic lipid having a protonatable tertiary amine.

We're not construing that claim. The *Moderna* Court addressed that limitation and the *Moderna* Court did not address "consisting essentially of", so it's a totally different argument then in the *Moderna* Court. But the point is clear, plaintiffs drafted this claim for the specific purpose of capturing defendants' product. There really can't be a dispute over that. And the real question is, did they make a mess of their patents by doing so, in view of the "consisting

essentially of" limitation.

And that's why our construction starts with indefiniteness, which, of course, we're not arguing today. And the core dispute is over the basic and novel properties. And our position is that the basic and novel properties are the stated advantages over the prior art in the specification. And plaintiffs' position is that it's the combination and concentration of the claimed lipid components. They said that's the basic and novel properties. And that's the dispute.

We rely on this case, *HZNP v. Actavis*. I'll refer to it as *Horizon*, because that's how they refer to it in the case. And the legal standard for "consisting essentially of", as counsel mentioned, is not in dispute. So I'm going to go to the next slide where the federal circuit in *Horizon* says: When you're looking to ascertain the basic and novel properties, you want to determine the goal of the invention, the goal, as distinguished from the prior art. Not a description of what's required to the claims, but why did the applicant get a patent? What's the goal of the invention? And how is it different from the prior art?

Now, the claims in the *Horizon* case are similar to the claims at issue here. They involve a formulation reciting components and concentration. Obviously, the specific type of formulation is different, but in essence, it's a formulation claim of components and concentrations just like what we have

here.

And then in the *Horizon* decision, the federal circuit talks about how the specification identifies a number of properties, advantages over the prior art, and identifies five: Transdermal flux, viscosity, stability, drying time, pharmacokinetics. And the Court found that the specification highlights these features as advantageous over the prior art. And with these particular aspects noted, the specification states that the invented formulation provides a superior means for delivery. And so the federal circuit said the district court thus correctly concluded that the intrinsic record identified these characteristics as the basic and novel properties. And this is exactly what we have here.

I'm on slide 59, looking at the '359 patent, column 5, line 54 to column 6, line 4. And here, the paragraph says: The present invention is based in part on the surprising discovery that the lipid particles comprising from about 50 mole percent have certain advantages. And, yes, it says the present invention is based in part. I mean, obviously, the present invention is also based on the components that's required in the claim. But they're saying an important part of the present invention is this surprising discovery, in the specification.

Counsel was saying we didn't cite anything in the prosecution history. It's in the specification itself, which

is more reliable than the prosecution history. And it's exactly what the *Horizon* case relied on.

And what are these advantages? One, increased activity of the encapsulated nucleic acid; two, improved tolerability of the formulations in vivo; three, significant increase in the therapeutic index; and four, stable or stability in circulation. Four basic and novel properties just like the basic and novel properties that were discussed in the *Horizon* case.

And you go on to the next paragraph, so on slide 60. And I've added column 6, lines 1 through 13. You can see that these advantageous properties are being compared to nucleic acid, lipid particles, compositions previously described, and they identify two of them. One of them has 30 mole percent cationic lipid, and one is 40 mole percent cationic lipid. I underline the 30 and the 40. And in the cite, we provide record cites for where these appear in the prior art. And so what the inventors are doing here is they're saying, surprisingly, when you use from about 50 mole percent of cationic lipid, you get these four advantages compared to the prior art. This is exactly what the inventors are saying in their specification.

And Counsel spent a long time, a long time addressing the comparator language in our proposed construction. Your Honor, that comparator language isn't -- you don't need to

decide that today. That may be relevant to indefiniteness. But I was looking at the *Horizon* case. And in the *Horizon* case, the construction was just the basic and novel properties are these five things. We think you can, as in *Horizon*, say the basic and novel properties are the four advantages that are in our construction. But what they are not is a combination and concentration of the lipid component. That's not a goal. That's just not a goal.

And counsel talked about how during prosecution there was a reference to a four-lipid composition. That's not a goal. There wasn't a stated goal to have only four lipids in the composition. Was there something wrong with five lipids in the prior art? There's no discussion of that. It's just a fact that it's a four-lipid composition. The goals are what are recited in the specification.

And that's my argument, Your Honor.

THE COURT: Thank you, Mr. Klein. No, I got it.

What else, folks? Anything else we need to talk about before I let you go home for the day?

Mr. Nimrod, do you have some brief reply from the plaintiffs' side? I will allow it.

MR. NIMROD: Just one thing, Your Honor. Couple things. The fact that we filed our patent application after their formulation came out, of course, the issue here is that that's irrelevant completely to claim construction. The fact

of the matter is that you can't just file a patent application and write these things in. When we filed that the examiner had to determine whether or not as of 2008 our patent described that invention. And the examiner decided that it did. So there's obviously nothing wrong with that. That was our invention, and we had a right to claim that.

Number two, the HZNP case is completely different here because in that case the descriptions of those five different parts, or advantages, were attributed to the claimed invention at issue in the case.

If you look at our situation here, Your Honor, their slide 60, if we look at it right now, it says in slide -- could we go to slide 60, please? Thank you.

It says: The present invention is based in part on the surprising discovery that lipid particles comprising from about 50 mole percent to 85 mole percent, and from about 13 to 49.5 percent mole percent, have certain advantages.

But is that the claim that's at issue here? Does the claim at issue recite 50 to 85 percent? No. Does the claim at issue here say 13 to 49 percent of the non-cationic? No. In fact, it says 30 to 55 percent.

So this is -- it's -- another example in column 18 at line 48 it says: In some embodiments the cationic lipid may comprise from about 50 percent. So it's just some embodiment. So question for Your Honor is whether this statement was

describing the claimed invention of the '378 patent. HZNP, it was, it was undisputed those statements related. This statement is not related to the claimed invention. The examiner didn't tell us to write 50 percent in. If we look at all of the statements here, the first sentence says: As relates to the embodiments that have 50 to 85 percent. Later it talks about some as illustrated in the examples herein. So that's a comparison of examples to something.

The last we rely on says: Is a non-limiting example, figure 3 of example 4 shows that one SLNP embodiment of the invention, 1:57, was ten times more efficacious as compared to a nucleic acid lipid particle previously described, 2:30. So that's one example. It's not saying the invention here is being distinguished over the prior art. It's not saying when you have an invention that has no cationic lipid limitation recited and allows for 30 to 55 percent, that we're going to distinguish it based on a ten times greater amount of efficaciousness, Your Honor. There's nothing in the record. They don't cite anything in the specification or anywhere else as to how that invention was distinguished. They're looking at a preferred embodiment, which is not the claims at issue here. That was prior patents. And those statements that were made are not applicable to the patents that are at issue today in terms of distinguishing over the prior art.

THE COURT: All right, thank you.

What else, folks? Anything we needed to address before I adjourn for the day from the plaintiffs' side? Aren't you guys tired of me already?

By the way, get a flavor of what it's going to be like if you guys want to try this case before me, because this is going to be the pace.

The only thing I'll promise is those chairs are coming in before January 6 because my trial -- I have an unrelated case going to trial January 6.

Is there anything further from the plaintiffs?

MR. NIMROD: No, Your Honor. Thank you, Your Honor.

THE COURT: Mr. Klein, anything further on behalf of the defendants?

MR. KLEIN: No, Your Honor, other than to point out that this is what they said in their application in 2008 and their claims required 50. And it's now today, after they know our molar ratio, they're saying, oh, no, our present invention is based on --

THE COURT: I got it. I understand the positions. Look, I'm reserving today, guys, I'm not going to decide from the bench. You've given me a lot to consider. It's going to take me some time to review the papers and also take into consideration your arguments and your positions today. But I appreciate it.

Anything else, though, Mr. Klein?

MR. KLEIN: Other than that, no, Your Honor.

THE COURT: Well, then I appreciate you guys being here. This has been helpful. And enjoy the rest of the day. We're adjourned. Be well.

THE COURTROOM DEPUTY: All rise.

(Proceedings concluded at 2:30 p.m.)

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FEDERAL OFFICIAL COURT REPORTER'S CERTIFICATE

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I certify that the foregoing is a correct transcript from the record of proceedings in the above-entitled matter.

/S/ Kimberly Wilson, RMR, CRR, RDR 12/28/2024

Court Reporter/Transcriber